Ocular Trauma
Series Editor: Hua Yan

Hua Yan
Editor

Ocular Emergency

Springer

Ocular Trauma

Series Editor
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Ocular trauma can be a serious threat to vision, especially if not medically intervened appropriately and in a timely fashion. Immediate and accurate diagnosis and effective treatment is the key to save the eyes and visual function, as well as a great challenge to ophthalmologists, especially emergency doctors. This book series is designed to help the doctors and clinical practitioners have a thorough understanding of ophthalmic emergencies and a mastery of every details of ocular trauma. To do the best, it is required that the ER doctors have solid theoretical knowledge about the anatomy of the eye and basic skills in ophthalmic operations. For that reason, "Anatomy and examination of ocular trauma" is believed to be necessary and fundamental for this book series. Beyond this, familiarity with the emergency room and efficient protocol will be helpful for the doctors to give treatment in the first time, and it will also be an important part of this book series. Almost all the aspects and details of ocular trauma will be covered in this book series, including mechanical and non-mechanical ocular trauma. Special topics of complicated situations, such as ciliary body impairment, will also be introduced in this book series. Hopefully the readers will enjoy it and find it helpful for them to provide better care to the patients and save vision.

More information about this series at http://www.springer.com/series/15621

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Preface

Ocular emergency involves a series of diseases that may take a heavy toll on visual function in a short period, thus requiring ophthalmologists to make diagnosis and give treatment timely and accurately to cut the patients' loss as much as possible, especially in the era of precision medicine. With the rapid development of science and technology, multiple advanced equipment have been used in clinical diagnosis and treatment. However, good theoretical knowledge and a streamlined clinical process are important to the prognosis of ocular emergency. With good theoretical knowledge, ophthalmologists can recognize the disease within a short time, and with a streamlined clinical process, ophthalmologists can give the most efficient management to the patient. For the ophthalmologists, especially for young ophthalmologists, a precise and high efficiency clinical process is essentially needed. Hence, this book may give a direction to them. The focus of this book is on the basic theoretical knowledge of ocular emergency, including the pathogenesis, manifestations, diagnosis, differential diagnosis, emergency treatment, and follow-up care, with a large amount of pictures and tables. It also focuses on introducing the emergency room and clinical process for young ophthalmologists who are just starting to comprehend ocular emergency.

The authors of this book are top-rated doctors and professors from around the world, including:

- Hong Yan, MD, PhD*, and Song Wang, MD (Chap. 1)
- Haoyu Chen, MD, PhD*, and Danny Siu-Chun Ng, MD (Chap. 2)
- Hua Yan, MD, PhD*; Jiaxing Wang, MD; Ying Li, MD; Xiangda Meng, MD, PhD; and Xuyang Yao, MD (Chap. 3)
- Bo Huang, MD, PhD* (Chap. 4)
- Gokhan Gurelik, MD*, and Huseyin Baran Ozdemir, MD (Chap. 5)
- Bo Huang, MD, PhD*, and Suxia Li, MD, PhD (Chap. 6)
- Ugur Acar, MD; Ahmet Murat Hondur, MD; and Gungor Sobaci, MD, PhD* (Chap. 7)
- Sengul Ozdek, MD*, and Ece Ozdemir, MD (Chap. 8)
- Weiyun Shi, MD, PhD*, and Suxia Li, MD, PhD (Chap. 9)
- Haoyu Chen, MD, PhD*; Dan Chao, PhD; Guihua Xu, PhD; Chen Lin, PhD; and Zeyi Li, MD (Chap. 10)
- *Corresponding author for each chapter

All of them have solid theoretical basis and abundant clinical experience. The authors' and their students' footprints cover the whole world including Asia, America, and Europe. Hundreds of thousands of patients' vision have been saved by them. In this book, they share the essence of their decades of clinical work and hope that it can help ophthalmologists to promote their diagnosis and treatment skills in ophthalmology emergency. However, because the book is highly professional and the authors focus differently, there may be some different opinions from doctors all over the world. And all the different views are welcomed and valued. We will be glad to discuss these with all colleagues.

Lastly, I hope this book can provide a reference for ophthalmologists to save more patients' visual function and can make a contribution to blindness prevention.

Tianjin, China Hua Yan

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1 General Guideline of Ophthalmic Emergency

Hong Yan and Song Wang

Abstract

In the situation of ocular emergency, rapid diagnosis and proper treatment are the key to success. First of all, the doctor should be familiar with common symptoms and signs in ophthalmic emergency, which include acute red eye, acute visual loss, acute ocular pain, ophthalmic trauma, and so on. From typical symptoms and signs, the doctor can make a quick judgment about the diagnosis. Then, the doctor needs to perform further examination to confirm the judgment. Evidence taken from patient history and specific ocular examination will support the doctor to make a correct diagnosis. Finally, in pursuit of the best prognosis, the doctor should make prompt and appropriate treatment. According to our experience, we have summarized the initial treatment for typical ocular emergencies as a reference. In conclusion, this chapter displays the standard procedure of dealing with ophthalmic emergency and tries to help doctors to build the pattern of clinical thinking.

Keywords

Ophthalmic emergency · Diagnosis · Examination · Treatment · Clinical thinking

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The subjects of ophthalmic emergency include acute illness, acute poisoning, and ophthalmic trauma. The research of etiology, pathogenesis, diagnostics, and treatment has significantly improved the outcome of ophthalmic emergency patients.

Rapid diagnosis and proper treatment are crucial for ophthalmologist to deal with ophthalmic emergency. In pursuit of the best prognosis, there are several basic principles to follow:

1. Immediate assessment of the patient's general and ocular conditions.
2. Making a correct diagnosis rapidly.
3. Developing a therapeutic strategy.
4. Proper medication.
5. Get ready for the patients with operation indications.
6. Mastering the principles and procedures of emergency surgery.
7. Consultation with doctors from related professions.
8. Be familiar with the laws that apply for emergency medicine.

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1.1 Common Symptoms and Signs in Ophthalmic Emergency

1.1.1 The Acute Red Eye

The red eye is red because its conjunctival vessels are engorged. These vessels may be engorged for many reasons, including inflammation of the eye or its surrounding structures or increased backflow pressure in its draining veins. In other words, a red eye could signify a problem with the eye, eyelids, lacrimal system, orbital soft tissues, or cavernous sinus. To sort through these conditions, use the diagnose tree in Fig. 1.1.

1.1.2 Acute Visual Loss

Acute visual loss that persists beyond 1 h requires immediate attention. The differential diagnosis includes keratitis, acute glaucoma, endophthalmitis, vitreous or retinal hemorrhage, retinal detachment, acute maculopathy, retinal artery occlusion, retinal vein occlusion, optic neuritis, ischemic optic neuropathy, occipital (visual) cortex infarction, and psychogenic visual loss. Table 1.1 compares symptoms, signs, and urgency of treatment for these conditions.

1.1.3 Acute Ocular Pain

Ocular pain may result from stimulation of trigeminal nerve fibers anywhere within the eye, the surrounding orbital tissues, and the base of the anterior or middle cranial fossa. If the pain arises from the eye itself, the eye (really the conjunctiva) will often be red. Pain that comes from a corneal epithelial defect feels like a grain of sand in the eye (foreign body sensation). If the pain arises from the eye's surrounding orbital tissues, eyelid swelling or proptosis is often evident. Deep orbital and intracranial processes causing pain, which often produce no external swelling, may cause Horner syndrome and impairment of the third, fourth, or sixth cranial nerves.

In ophthalmic emergency, acute ocular pain is usually associated with conditions from these categories:

1. Corneal or eyelid abnormality and diffuse conjunctival congestion
2. Drastic increase in intraocular pressure such as acute angle-closure glaucoma, traumatic glaucoma, pigmentary glaucoma, uveitis, and hyphema
3. Ciliary injection such as scleritis, uveitis, and endophthalmitis

1.1.4 Ophthalmic Trauma

Quick action is often called for in managing ocular injury. Some cases should be treated on the spot. Other cases should be referred promptly because of the difficulty in diagnosis and management and the potential threat to sight.

Ophthalmic trauma in emergency could be classified as below:

1. Mechanical injuries which include blunt injury, lamellar laceration, rupture of the globe, penetrating injury, intraocular foreign body, and perforating injury.
2. Nonmechanical injuries like chemical burn, thermal burn, and radiation injury.

1.2 The Clinical Thinking of Ophthalmic Emergency

In all the situations of ophthalmic emergency, there are only two conditions that need to be treated within minutes—chemical burn and retinal artery occlusion—while in some conditions like endophthalmitis, intraocular foreign body, and orbital cellulitis, medical intervention should be introduced within hours. In certain cases, consultations with other professionals (radiologist, otolaryngologist, and neurologist) are necessary.

Ocular trauma is very common in emergency room. When dealing with trauma patients, ophthalmologists should check the patient's gen-

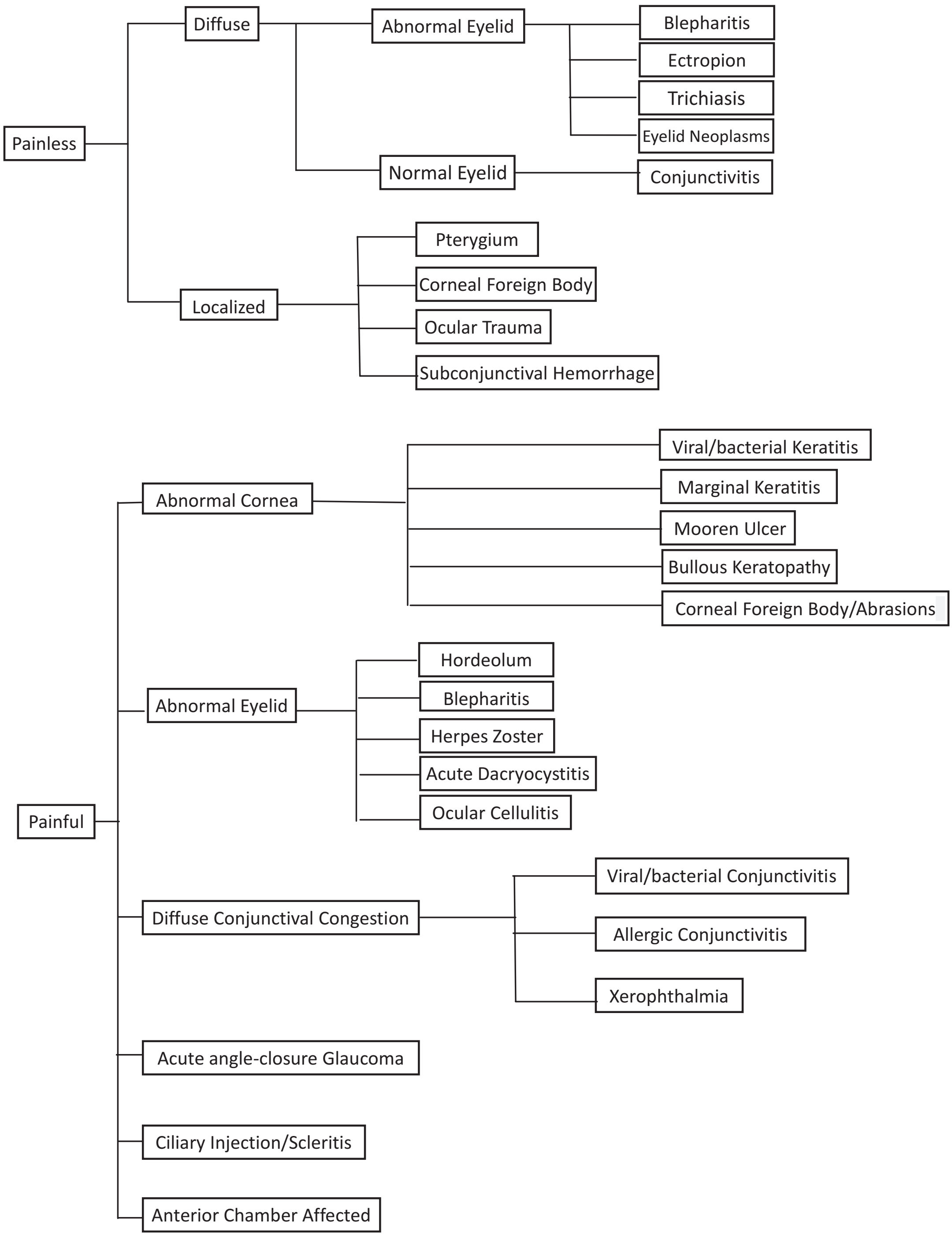

Fig. 1.1 Acute red eye

Table 1.1 Differential diagnosis of acute visual loss

Condition	Pain	Red eye	Afferent pupil defect	Ophthalmoscopic findings	Urgency of treatment
Keratopathy	+	+	–	–	**Emergent**
Acute angle-closure glaucoma	+	+	+/–	–	**Emergent**
Endophthalmitis	+	+/–	–	**Reduced red reflex**	**Emergent**
Retinal or vitreous hemorrhage	–	–	–	**Reduced red reflex (if vitreous hemorrhage is extensive)**	**Urgent**
Retinal detachment	–	–	+/–	**Retinal separation**	**Emergent**
Acute maculopathy	–	–	–	**Altered color in macula**	**Urgent**
Retinal artery occlusion	–	–	+	**Cherry-red spot**	**Emergent**
Retinal vein occlusion	–	–	+/–	**Retinal hemorrhage**	**Urgent**
Optic neuritis	+	–	+	**+/– swollen disc**	**Urgent**
Ischemic optic neuropathy	–	–	+	**Swollen disc**	**Emergent**
Occipital (visual) cortex infarction	–	–	–	–	**Urgent**

Emergent = within 24 h; urgent = within 48 h

eral conditions thoroughly. Combined injuries and multiple injuries are quite normal among patients suffering from car accidents and explosive injuries. The top priority in treating these patients is to check their vital signs and organs. If the patient's signs are critical, ophthalmologists should quickly transfer the patient to a surgeon for further inspection. When the patient's injuries are confined to the ocular, emergency doctors need to be careful with wounds caused by foreign body whose physical signs may be slight but may seriously threaten vision if left in place.

In general hospital, trauma patients that require multiple specialists from different professions are not unusual. In these cases, doctors must cooperate as a team in order to do their work efficiently. Emergency consultations with ophthalmologists can be decisive in the diagnosis of certain diseases such as papilledema, craniofacial trauma, vascular disease, and toxemia of pregnancy.

Figure 1.2 is the routine procedure of ophthalmic emergency. It will help the doctor to get a general assessment of the emergency patient.

1.3 Key Points of Examination in Ophthalmic Emergency

1.3.1 History

In most circumstances, the first step of treating an emergency patient is to acquire the patient's detailed medical history. Information like visual acuity prior to and immediately following the injury, the time of injury, the mechanism of injury, and previous history is crucial for further inspection and treatment.

The details of the injury are very important for the assessment of ocular trauma patients. The questions below are helpful for ophthalmologists in the process of history taking:

- Did the patient feel a sudden impact on the eyelids or eye?
- Was the patient wearing glasses or goggles?
- Does the patient complain of pain or decreased vision?
- What object struck the patient?

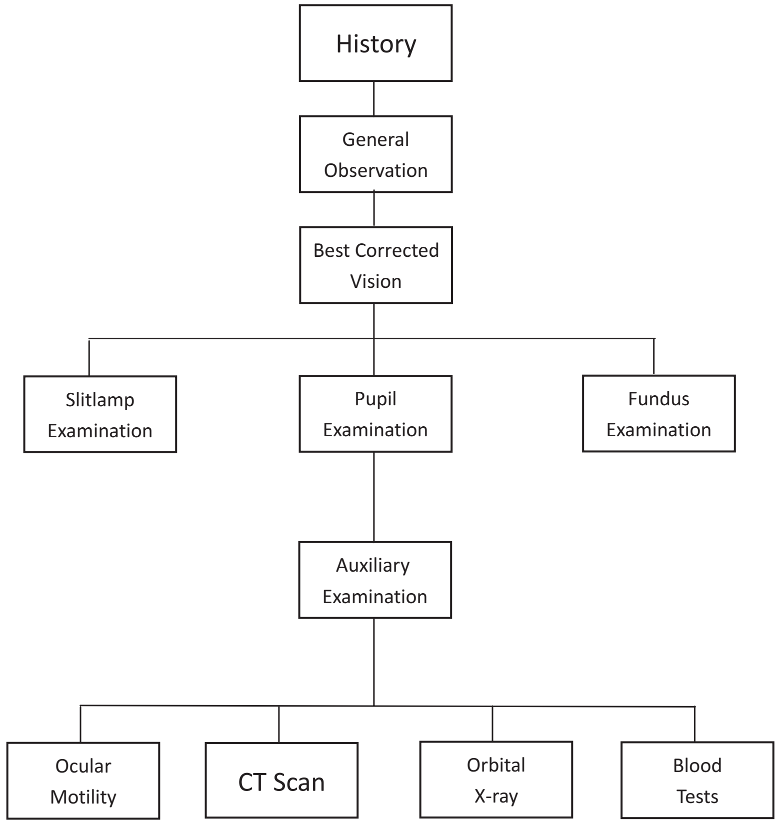

Fig. 1.2 Routine procedure of ophthalmic emergency

- How was the patient struck?
- How long ago did the injury occur?
- Does the patient have lingering vision impairment, diplopia, or severe pain?
- When was the last time that the patient got vaccinated against tetanus?

3. The patient's general condition, systemic disease, and medication use need to be recorded particularly.
4. A well-written medical record is not only convenient to read and communicate but also an important part of legal instruments.

Key Points

1. A good history taking is the first step of successful treatment.
2. If the patient's only healthy eye is injured, the treatment should be cautious. Consultation with senior doctors is necessary.

1.3.2 Ocular Examinations

It is important to make a routine procedure to assess the patient's conditions comprehensively. Both eyes need to be checked thoroughly. For multiple injury patients, vital signs should be checked first. When the patient's signs are steady, ocular examinations could follow up. When a

patient has chemical burn, the first thing to do is irrigating. If the patient's symptoms suggest infective conjunctivitis, mydriasis is not recommended at the time.

1.3.2.1 Visual Acuity

Measuring visual acuity is the first and foremost test for ophthalmic emergency patients. Severely injured or immobilized patients could use near vision test to record. If the patient cannot see the largest Snellen letter, alternative tests (counting finger acuity, hand movement acuity, and light perception acuity) should be performed to assess the patient's eyesight. For presbyopia and aphakia patients, their corrected visual acuity should be recorded.

Key Points

1. The patient's both eyes need to be checked.
2. For patients with severe visual loss, visual acuity test is crucial for the assessment of their vision prognosis.
3. Visual acuity test is an important part of legal instruments for cases that may involve in legal disputes.
4. Topical anesthetics can greatly help the test of patients who have difficulty in opening eyes.
5. Even though the patient's eyesight is normal, there still may be underlying sickness within the eye.

1.3.2.2 External Examination

Many ocular traumas and emergencies can be diagnosed by inspection of the facial and periorbital area. Symptoms and signs like exophthalmos, enophthalmos, skin ecchymosis, periorbital emphysema, ptosis, and numbness of the infraorbital should be noticed.

Under direct penlight illumination, doctors should inspect the eyelid, lacrimal apparatus, and eye muscles. After inspection, details such as the injured place, range, severity, and complications need to be carefully recorded and drawn.

Key Points

1. Any laceration should estimate the depth of the wound and describe the adjacent tissue's situation especially lacrimal apparatus's condition.
2. Palpate the rim of the orbital bone to see whether it is irregular to identify fractures.
3. Enophthalmos indicates rupture of the globe or orbital fractures, while exophthalmos suggests orbital hemorrhage.
4. Numbness of certain facial area indicates the fracture sites.
5. Subcutaneous emphysema in the eyelid and ocular adnexa indicates medial wall or floor fracture in the orbit.

1.3.2.3 Pupillary Examination

Pupillary examination offers objective evaluation of the condition of the visual pathway. The pupils should appear symmetric, and each one should be examined for size, shape (circular or irregular), and reactivity to both light and accommodation. Pupillary abnormalities may be due to neurologic disease, acute intraocular inflammation, and ocular trauma.

Key Points

1. The size of the pupil is an important indication of cranial nerve involvement.
2. The shape of the pupil offers information about iris damage, detached vitreous body, and intraocular foreign body.
3. In traumatic cases, relative afferent pupil defect (RAPD) is usually a sign of a unilateral optic nerve lesion or of bilateral but asymmetric optic nerve lesions.

1.3.2.4 Visual Fields

When treating ocular emergencies, confrontation visual field test can be used to detect gross visual pathway disturbances. This test measures the patient's ability to use peripheral vision to iden-

tify large targets. More definitive visual field testing employs instruments called perimeters.

1.3.2.5 Ocular Motility

The objective of ocular motility testing is to evaluate the alignment of the eyes and their movements, both individually and in tandem. If the patient's situation involves orbital injury or cranial nerve injury, it is important to test the patient's ocular motility.

Key Points

1. The decrease in ocular motility indicates rupture of the globe or orbital fractures.
2. The paralytic or restricted eyeball movement can be identified by forced duction test. If it is open wound, the test should be delayed.

1.3.2.6 Anterior Segment Examination

If the patient's condition is stable and convenient, slit lamp is the best option to inspect the patient's anterior segment. The direct ophthalmoscope is alternative. The examination should be organized in order:

eyelashes → eyelid → conjunctiva → sclera → cornea → anterior chamber → iris/pupil → lens.

1.3.2.7 Posterior Segment Examination

Since ocular emergency patient's conditions could be complicated, the patient's posterior segment should be thoroughly checked as soon as possible. If the process is delayed, situations like corneal decompensation, vitreous hemorrhage, endophthalmitis, and hyphema may further affect the examination.

Key Points

1. Before mydriasis, the patient's iris and pupil should be inspected.
2. If the patient's head or iris is injured, mydriatic should be forbidden.
3. The patient's usage of mydriatic needs to be recorded carefully, especially when the patient's head is injured.

1.3.2.8 Intraocular Pressure

The change of intraocular pressure (IOP) is a reminder of certain disease. The decrease of IOP is a sign of situations like retinal detachment, traumatic iridocyclitis, cyclodialysis, and perforating globe injury. Increased IOP are usually linked with disorders like glaucoma, hyphema, and uveitis.

Key Points

1. Decreased IOP is an important clue to search for hidden wounds in perforating globe injury.
2. The increase of IOP cannot rule out the possibility of eyeball rupture.
3. In case of acute angle-closure glaucoma, patient's IOP could increase drastically, which calls for immediate medical intervention.

1.4 Treatment of Ocular Emergencies

The outcome of ocular emergencies depends on timely management, which makes prompt and appropriate treatment essential in the primary care setting. Chemical burns, penetrating globe injuries, central retinal artery occlusion, acute angle-closure glaucoma, and retinal detachment are the most common and urgent cases for ocular emergency. In these circumstances, patients need to be transferred immediately to the emergency department or an ophthalmologist. In Table 1.2 [1], the initial treatment of these situations is summarized.

1.4.1 Penetrating Globe Injuries

(a) Leave the foreign object in situ since removal may lead to further herniation of the eye con-

Table 1.2 Initial treatment of ocular emergencies

Disorder	Initial treatment
Penetrating globe injuries	Eye shield; tonometry contraindicated
	Leave embedded foreign object in place
	Scheduled analgesia and antiemetics
	Update tetanus immunization
	Immediate referral to an ophthalmologist
Retinal detachment	Antitussives or antiemetics (if needed)
	Referral to an ophthalmologist within 24 h
Central retinal artery occlusion	Lowering IOP with mannitol (Osmitrol) 0.25–2.0 g per kg IV once
	Acetazolamide (Diamox[a]) 500 mg IV or orally once
	Carbogen inhalation
	Administering oral nitrates or by laying the patient on his or her back
	Ocular-digital massage
	Immediate referral to an ophthalmologist
Acute angle-closure glaucoma	Lowering IOP with acetazolamide 500 mg orally once
	One drop each of 0.5% timolol maleate (Timoptic), 1% apraclonidine (Iopidine), and 2% pilocarpine (Isopto Carpine) 1 min apart and repeated three times at 5-min intervals
	Immediate referral to an ophthalmologist
Chemical burns	Eye irrigation with normal saline or lactated Ringer's solution until pH is normal
	Continue eyewash on the way to the emergency department or an ophthalmologist

IOP intraocular pressure, *IV* intravenously
[a]Brand only available in the oral formulation

tent. Do not touch or manipulate the injured eye.

(b) Auxiliary medicine like antiemetics, topical anesthetics, and antibiotics can be given to suppress vomiting, aid comfort, and reduce the risk of infection. Tetanus status should be confirmed and a booster dose given if required [2].

(c) Advise the patient to avoid movement that may deepen the wound before seeing a specialist. Eating or drinking should be forbidden since surgery is often required in this situation.

(d) Eye shields, instead of pressure patch, can be placed over the injured eye to offer protection. The bottom of a disposable cup can be used as substitute.

1.4.2 Retinal Detachment

(a) Patient history is crucial in making the diagnosis. Symptoms of "flashes and floaters," especially progressive onset of symptoms, are often recorded.

(b) Patients may also describe a "cloud" or "web" over their vision as the detachment progresses. A recent history of ocular trauma or surgery is commonly related to the sickness [2].

(c) Instant referral to an ophthalmologist is required if a retinal detachment is diagnosed.

(d) The best treatment for retinal detachment is surgery, including pneumatic retinopexy, scleral buckle, pars plana vitrectomy, or a combination of these methods.

1.4.3 Central Retinal Artery Occlusion

(a) Transfer the patient with symptoms and signs of central retinal artery occlusion (CRAO) immediately to an ophthalmologist since irreversible damage occurs in 100 min after occlusion [1].

(b) Initial treatment of CRAO includes the acute presentation of inhalation (95% O_2 and 5% CO_2), laying the patient flat on his or her back, administering oral nitrates, or ocular-digital massage.

(c) Timely treatment is the first priority, and there is no clear evidence to recommend one treatment over another for acute CRAO.

1.4.4 Acute Angle-Closure Glaucoma

(a) Lowering the intraocular pressure is the centerpiece of all the clinical treatment.
(b) Before seeing an ophthalmologist, the following procedures are highly recommended: give the patient eye drops (0.5% timolol maleate, 1% apraclonidine, or 2% pilocarpine) for three times at 5-min intervals; take a 500-mg tablet of acetazolamide; measure the patient's intraocular pressure every hour [1].
(c) Laser or surgical iridectomy is the definitive treatment for primary acute angle-closure glaucoma.

1.4.5 Chemical Burns

(a) Instant and sufficient irrigation is the most important treatment for chemical burns.
(b) Lactated Ringer's solution, normal saline, or water can be used as irrigation solutions. The injured eye should be irrigated with at least 2 L of fluid.
(c) The pH of the ocular surface should be strictly monitored, and a wet cotton swab can be used to sweep the upper and lower fornices to remove any retained crystallized chemical particles.
(d) For mild burns, treatment with antibiotic eye drops and artificial tears is sufficient for corneal and conjunctival epithelial healing. In severe cases, topical steroid, ascorbate, and citrate drops should be added to reduce inflammation and promote epithelialization [3].

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2 Emergency Room (ER)

Haoyu Chen and Danny Siu-Chun Ng

Abstract

The design of the emergency rooms needs to be comprehensively considered. Some general principles, such as accessibility, signage, and good relationship with other departments, should be considered. There are also some special instruments, drugs, and common supplies needed in the ocular emergency rooms. In an eye hospital, the emergency room should have some essential setting for examination and management of systemic emergency. Patients coming to the emergency room are mixed with different levels of severity and crisis. They should be managed differently according to their specific situations. First aid is needed for the following conditions: chemical injury, open globe injury, and acute painless vision loss. Hospital-acquired infection is a major challenge in high turnover emergency rooms. The following strategies should be used for infection control: hand hygiene, separate infection source from the rest of departments, healthcare personnel protection, and environment controls.

Keywords

Emergency rooms · Setting · Triage · First aid · Infection control

Emergency room is essential in any healthcare system. It provides immediate management for patients suffering from serious, acute ocular illness. The design of the emergency rooms needs to be comprehensive. There are many things which should be considered. First, the design must follow some general requirements, including the location, accessibility, privacy, infection control, and so on. Second, there are some special design, instruments, drugs, and supplies for the ocular emergency room. Third, in eye hospital, there may be some patients with life-threatening systemic emergency and need immediate management. Therefore, the emergency room in eye hospital must have some instruments and drugs for diagnosis and management of systemic emergency.

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2.1 General Consideration Is Designing Emergency Rooms

Emergency rooms have some specific purposes which should be considered in its design.

1. The patients are usually in acute condition and need immediate care.
2. The patients and companions are usually stressed and anxious.
3. The patients have different severities and levels of emergency.
4. The triage and discharge pathways of patients may vary.

Therefore, there are some general considerations:

1. Accessibility. The emergency room should locate near the front door. And the front door can be assessed by ambulance or other vehicle transporting the emergency patients. So the patients in acute condition can arrive at the emergency room in the shortest time.
2. Signage. Clear signage of emergency room should begin outside the hospital to guild the patients/drivers to the emergency room. Inside the department, signage about the patient pathway, services, and facilities should be clear. Braille for visually impaired patients should be used [3].
3. Good relationship with other departments. The patients may need further investigation and/or admission. Therefore, the emergency rooms should have access to these modalities, including radiology, ultrasound, CT scanning, clinical chemistry lab, inpatient wards, operating theatre, pharmacy, etc. Signage, clear unencumbered route, and information technology communication are necessary in connecting the relationship.
4. Other general requirements: clean and well-maintained environment; noise control, with stereo system playing calming and non-repetitive music; appropriate room temperature; adequate space for waiting patients and companions; information kiosks; and health education magazines or television.

2.2 Instruments, Drugs, and Common Supplies in the Ocular Emergency Rooms

Ocular emergency rooms should include at least an examination room and a treatment room. The room should have enough lighting but also have curtain to keep the room in dark when the light turned off. If there is enough space, the examination room can be separated into two independent rooms, the consultation room and examination room. The consultation room is for consultation and examination by physicians. While the examination rooms have the examination instruments performed by nurse or technicians.

2.2.1 The Examination Room Should Have the Following Instruments

1. Visual chart. The room should have enough space for visual examination, which depends on the type of visual chart used. The visual chart can be Snellen, ETDRS, or any other charts commonly used in local practice. Near visual chart should also be supplied to differentiate myopia and other diseases.
2. Tonometry. Usually noncontact tonometry is used. However, some patient may have uneven ocular surface or extremely high or low intraocular pressure. Noncontact tonometry can be inaccurate in these conditions. Tono-Pen or ICare tonometry can be used in these cases and should also be available.
3. Refraction instruments. Auto refractometer or kerato-refractometer can objectively read the refraction of the eye in a short time. Trial frames

and trial lens sets can help to measure the best corrected visual acuity. Lensmeter can read the power of the lens wearied by the patients.

4. Flashlight. Although flashlight is simple, but it is very useful and should not be forgotten in the inventory. It can be used to assess whether the patient has light perception and light projection. Using flashlight and a pair of red/green lens, simple color vision can be tested. Furthermore, it can be used to exam whether the patient has strabismus and how is the eye movement. Last but not least, it can exam direct/indirect pupil reflex and relative afferent pupil defect.
5. Slit lamp microscopy. Although any brand of slit lamp microscopy can be used in the consultation room, it is recommended using the ones with digital camera to record the lesions on anterior segment. We also suggest that a portable slit lamp microscopy be supplied, because some patients may not be able to sit in front of an instrument. Portable slit lamp microscopy is especially useful for these patients.
6. Direct or indirect ophthalmoscopy. It is recommended the models come with battery and can be easily used without limitation to the examined desk. Direct ophthalmoscopy has advantage of high resolution but only for a small field. While indirect ophthalmoscopy has the advantage of wide-field and stereo view. Direct ophthalmoscopy is useful for macular disease, while indirect one is better for peripheral retinal diseases.
7. Contact and noncontract slit lamp lens. The contact slit lamp lens includes goniolens and Goldmann three-mirror lens. They are used to examine the anterior chamber angle and retina. The noncontact slit lamp lens includes models with different power, which have different magnifications and fields of view. They are used for macula/optic disc or peripheral retina examination, under different sizes of the pupil.

2.2.2 The Following Drugs or Consumables Should Be Supplied in the Examination/Consultation Rooms

Drug/consumable	Effect
Anesthetic eye drop	Some patients may have eye pain and cannot cooperate with examination. Topical anesthesia can relieve the symptom and help the examination
Fluorescein strips	Examination of corneal epithelium damage, leakage of wound
Mydriatic eye drop	To dilate the pupil for examination of the retina
Myotic eye drop	To contract the pupil in patients with acute angle closure
PH papers	To examine the PH value in chemical injury

2.2.3 Setting for Ocular Treatment Room

1. The ocular treatment should locate near to the consultation room. Some patients may need immediate eye washing and can be transported from the consultation room to treatment room in the shortest time.
2. There should have adequate lighting. Shadowless lamp should also be supplied to illuminate the field of treatment/operation. Electric power outlet should be provided.
3. Therapeutic bed and therapeutic chair.
4. Surgical microscopy: it would be better to have a surgical microscopy so some emergent surgical management can be performed. It doesn't need to be an advanced model, but a simple surgical microscopy is enough (Fig. 2.1).
5. Surgical table and chairs.

Fig. 2.1 Surgical microscopy and surgical table

6. Surgical tools: the autoclaved surgical tools can be packed and ready for used.
7. Syringe and needles: with different sizes and gauges.
8. Changing and packing.
9. Disinfection reagents: 75% alcohol, 2% H_2O_2, povidone iodine. The room should have a UV light and disinfection at least 30 min, twice a day.
10. Washing set and washing solution: 9% NaCl for regular washing, 2% boric acid for alkali burn, 2% $NaHCO_2$ for acid burn.
11. Garbages for biohazard waste and non-biohazard waste. They should be separated and have clear signs.

2.2.4 Setting for Management Systemic Emergency in Eye Hospital

It must be kept in mind that some patients may develop or have pre-existing systemic disorders. For example, a patient receiving intravenous injection of fluorescein may develop allergic reaction, even shock. Some systemic disease may need emergency management. In general hospital, these conditions can be managed by other subspecialties. However, the emergency room in eye hospital should have some essential setting for examination and management of systemic emergency.

The essential instruments include:

1. Multifunction monitor. The device has multiple functions, including blood pressure measurement, electrocardiogram monitor, and pulse oximeter monitor.
2. Blood pressure meter. Although blood pressure can be measured with the monitor, an independent automatic or manual blood pressure is also needed to measure the blood pressure at the other limbs if needed. Furthermore, there may be more than one patient who needs measurement of blood pressure.
3. Electrocardiogram. Electrocardiogram can be shown on the monitor; however, it usually only demonstrates one or two channels. A standard 12-channel electrocardiogram is essential to identify heart diseases.
4. Defibrillator. Defibrillator is an important therapy for patients with life-threatening cardiac dysrhythmias, specially ventricular fibrillation and ventricular tachycardia. It can convert these dysrhythmias to normal electrocardiogram. It can be combined with the multifunction monitor or be an independent instrument.

5. Oxygen tank and mask. Oxygen supply is not only essential for patients with respiratory distress but also an important therapy for patients with central or branch retinal artery occlusion. Although central supply is a safer method for oxygen delivery, oxygen tank is needed for patients with immediate need and cannot be transported to the oxygen outlet.
6. Electric suction apparatus. The opening of airway is critical. Some patients may have airway obstruction by foreign body, sputum, etc. Electric suction apparatus help to clean the airway and keep it open.
7. Ventilator. It is a machine designed to help breathing for a patient who is in respiratory failure, due to central nerve system disorders or others. Ventilator is essential to provide sufficient oxygen for the need of the body in these patients.

In emergency, some drugs are needed to be administered to patient within a short time without delay from delivery from the pharmacy. Following are some examples of drugs which should be stored in the emergency rooms.

Drugs		Effect
Inj. Lidocaine hydrochloride	0.1 g/5 ml	Local anesthetic surgery
Inj. Calcium gluconate	1 g/10 ml	Hypocalcemic tetany, magnesium sulfate overdose, allergy, etc.
Inj.50% glucose	10 g/20 ml	Hypoglycemia
Inj. Amiodarone	150 mg/3 ml	Arrhythmia
Inj. Sodium nitroprusside	50 mg	Hypertension
Salbutamol sulfate inhaler	100 mg	Wheezing and shortness of breath
Inj. Furosemide	20 mg/2 ml	Congestive heart failure, edema, etc.
Inj. Aminophylline	0.25 g/2 ml	Asthma, emphysema, bronchitis
Inj. Diazepam	10 mg/2 ml	Anxiety disorders, muscle spasms, seizures
Tab. Nitroglycerin	0.5 mg	Hypertension, CRAO
Inj. Nitroglycerin	5 mg/1 ml	Hypertension, CRAO
Inj. Phentolamine mesylate	10 mg/1 ml	Hypertension, CRAO
Inj. Metaraminol bitartrate	10 mg/1 ml	Hypotension, shock
Inj. Nikethamide	0.375 g/1.5 ml	Respiratory arrest
Inj. Lobeline	3 mg/1 ml	Respiratory arrest
Inj. Dexamethasone	5 mg/1 ml	Allergy, stress, inflammation
Inj. Promethazine	50 mg/2 ml	Allergy, nausea and vomiting, sedation
Inj. Epinephrine	1 mg/2 ml	Hypotension, shock
Inj. Isoprenaline	1 mg/2 ml	Hypotension, shock
Inj. Norepinephrine	2 mg/1 ml	Hypotension, shock
Inj. Atropine	0,5 mg/1 ml	Pylorospasm, ureteral and biliary colic, mushroom poisoning due to muscarine
Inj. Deslanoside	0.4 mg/2 ml	Congestive heart failure, cardiac arrhythmia
Inj. Dopamine	20 mg/2 ml	Shock

In addition, some common supplies should also be stored in the ER, including syringes, cotton swabs, adhesive tapes, blood collection needle and tubes, infusion tubes, three-way stopcocks, pads, connecting tubes, heparin plugs, 18 G needles, trocars, tourniquet, povidone, tapes, medical bottle opener, scissors, thermometer, bottle opener, flashlight, tracheostomy set, vein incision kit, tongue forceps, mouth gag, tongue blade, sterile towels, urinary catheterization set, gloves, oxygen tubes, oxygen masks, bandage, electrode slice, tracheal cannula, breathing pipe, suction tubes, blood sugar tester, stethoscope, power strip, etc.

Due to the large variety of drugs and supplies required to be stored in ER, it is important to store them with good organization. An emergency cart with several layers, trays, and drawers will help to organize the storage. The wheel

Fig. 2.2 An emergency cart with several layers, trays, and drawers help to organize the storage of drugs and supplies needed for management of crisis

underneath will help to move it to any patient in crisis (Fig. 2.2).

2.3 Triage

The patients coming to emergency room are mixed with different levels of severity and crisis. They should be managed differently according to their specific situations [1]. The nurses at the reception desk should immediately assess the patients upon arrival. Patients can be tagged with different colors, which represent different levels of emergency. The triage area or reception desk should be located at the entrance of emergency rooms. Following are examples of codes or tags used for different patients.

1. Red tags: The patients are critical and need immediate treatment. They must be seen by doctor immediately. They can be directly sent to the treatment room. Inform doctor and other nurses. Registration can be made after or at the meantime of immediate management.
   (a) Chemical injury
   (b) Patients with systemic criticism
2. Yellow tags: For the patients who need acute but not immediate management. Registration can be made after or at the meantime of immediate management.
   (a) Central retinal artery occlusion and branch retinal artery occlusion
   (b) Acute angle closure or other acute glaucoma
   (c) Open globe injury
   (d) Endophthalmitis and orbital cellulitis
3. Green tags: For the patients who are not seriously sick and don't need acute management within 1 h.
   (a) Acute red eye
   (b) Closed globed injury
   (c) Uveitis and scleritis
   (d) Orbital injury
   (e) Retinal detachment
   (f) Optic neuropathy
   (g) Retinal vein occlusion
   (h) Vitreous hemorrhage
   (i) Conjunctivitis
   (j) Keratitis
   (k) Ocular surface injury
   (l) Subconjunctival hemorrhage

2.4 First Aid in the Ocular Emergency Rooms

2.4.1 Chemical Injury

When chemical injury is suspected, immediate management should be started. PH paper should be used to test the PH value of conjunctiva. Then the eye should be irrigated with at least 500 ml solution. PH test will be repeated. More solution irrigation if the PH value is still not normal.

Topical anesthesia can be used to relieve any irritating sensation. A speculum should be used to open the eyelid. Careful examination should be performed to look for any possible foreign body in conjunctival sac. If present, remove it.

2.4.2 Open Globe Injury

The first thing for mechanical injury is to exclude severe systemic injury, whether there is severe injury of the brain, neck, chest, or abdomen and whether the vital signs are stable. If there is severe systemic injury, immediate management for systematic conditions should be started. At the meantime consult and refer to other subspecialists.

After exclusion of severe systemic injury, the eye should be examined with caution. Don't push the eye to avoid further prolapse of intraocular tissue. Don't use eye drops before surgery to avoid the toxicity of topical medicine. For pediatric patients, fasting should be initiated to prepare for general anesthesia.

2.4.3 Acute Painless Vision Loss

Careful examination is needed to differentiate the pathology that contributes to the vision loss. Common causes include retinal artery occlusion, retinal vein occlusion, retinal detachment, vitreous hemorrhage, choroidal neovascularization with and without subretinal hemorrhage, anterior ischemic optic neuropathy, optic neuritis, cerebrovascular disorder, and hysteria. Mydriasis should not be regularly performed before examination of pupil reflex, visual field, and visual evoked potential.

Immediate management is needed for retinal artery occlusion. Attention should be paid to the neurological signs. If there is positive finding, consultation with neurologists is recommended.

2.5 Infection Control in Emergency Room

Hospital-acquired infection is a major challenge in the high turnover emergency rooms. The patients in emergency room may carry pathogens which can be transmitted to not only other patients but also healthcare personnel. Following are some important strategies to prevent infection.

2.5.1 Hand Hygiene

The hands of the healthcare personnel are the most common vehicle of hospital-acquired infections. Therefore, hand hygiene is the primary prevention strategy. Hand hygiene includes hand washing and hand disinfection. It should be performed immediately after gloves removed, between patient contacts, after contamination of blood, secretions, body fluid, tissue, and instrument.

Hand washing should use antibacterial soap or alcoholic solution, but not non-medicated soap. Alcohol-based gel or foam products are superior to regular and antimicrobial soap. It also takes less time using gel or foam in comparison with water and soap. This would improve adherence to hand hygiene [2].

2.5.2 Separate Infection Source from the Rest of Departments

The patients with infectious eye diseases must be managed with caution, including conjunctivitis, keratitis, endophthalmitis, and orbital cellulitis. Preferably, there should be an independent room for examination and consultation of these kinds of patients, especially during an epidemic of conjunctivitis. Careful cleaning and disinfection should be performed after examination of the patients, including healthcare providers' hands, devices such as slit lamp microscopy, and so on.

For the patients with only monocular involvement, examination should be performed firstly on the contralateral eye and then the disease eye. Use independent material for unilateral ocular infection. Beware that tear can be the source of infection.

2.5.3 Healthcare Personnel Protection

Gloves should be worn when the healthcare personnel touch body fluids, blood, secretions, excretions, and potential contaminated items. Mask, protecting glasses, or face shield should

also be worn to protect the eye, nose, and mouth when there is high risk of contamination by sprays or splashes of body fluid, blood, secretions, and excretions.

Take care to prevent occupational health injury, especially when using needles, scalpels, and other sharp instruments or devices. The patients in emergency rooms may need immediate management before the result of the test for human immunodeficiency virus, hepatitis B virus, hepatitis C virus, and other diseases come out. Immunization is an important strategy to protect healthcare personnel for HBV. In case that healthcare personnel with anti-HBs Ab negative is injured by instrument potentially contaminated with HBV, they should receive HBIG or antivirus medication. If injured by instrument potentially contaminated with HIV, the healthcare personnel should receive antivirus therapy immediately.

2.5.4 Environment Controls

The environmental surfaces and medical instrument may be contaminated after contact with patients. Therefore, proper cleaning and disinfection should be performed. Slit lamp microscopy should be disinfected with alcohol between patients. UV light disinfection should be performed twice a day for the environment surfaces.

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Patient Care Process of Ocular Emergency

3

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Abstract

In case of ocular emergency, prioritization is of great importance. A well-organized patient care process will save time and alleviate the patients' suffering to a great extent. In this chapter, the general patient care process of various ocular emergencies including ocular trauma, chemical burn, and other common ocular emergencies is discussed in a step-by-step manner, from initial consultation with an ophthalmologist to treatment and follow-up. Patient care process on special events such as mass casualty is also well discussed. A recommended flowchart is provided for each case to help the clinicians and nurses keep a clear mind and make proper decisions from the chaos of ocular emergency.

Keywords

Patient care process · Prioritization · Ocular trauma · Chemical burn · Mass casualty · Flowchart

As a doctor or a nurse, facing a patient with urgent complaint about the eye, a lot of things you have to do will come to your mind all together. Such things have different priorities in different cases, and the medical staff should have a well-organized patient care process which will help to save time and alleviate the patients' suffering to a great extent. Recommended general patient care process of various ocular emergencies, as well as patient care process on special event such as mass casualties, will be discussed

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in this chapter. Differential diagnosis and treatment in details of each ocular emergency will be discussed in other chapters of this book, but not this chapter.

3.1 Ocular Trauma

- **Step 0: Before ophthalmologist**

Before ophthalmologist, vital signs of the patient should be checked to make sure no current or hidden life-threatening conditions present.

- Check pulse rate, respiration rate, and blood pressure.
- In many cases, ocular trauma can be accompanied by other types of trauma which may be hidden but life-threatening. Traumatic brain injury (TBI) is the most common and the most dangerous case, including hematoma, hemorrhage, skull fracture, etc. [1]. Doctors should pay special attention to the cause of injury and the current consciousness of patient. It is recommended to use Glasgow Coma Scale [2] to evaluate patient's consciousness in ocular trauma combined with TBI.
- Stop bleeding if bleeding from skin wound (no pressure on the eyeball if open globe injury is suspected).
- CT examination for the brain can be done before the ophthalmologist if necessary.

- **Step 1: Quick examination and quick history**

The quick examination and quick history can be done within 2 min, to help you make a quick triage of the condition and decide the urgency of this case.

- Quick examination:
  - VA by counting finger or hand motion
  - First look of the eye by flashlight, pupil reflex included
- Quick history, questions to ask:
  - What is your name?
  - How did it happen?
  - When did it happen?
  - Is there any other wounded?

- **Step 2: Calm and stabilize the patient**

Initial treatment aimed to make the patients relieved from the pain and suffering as soon as possible so they can be calm and cooperate to the next detailed examination and history. The initial treatments usually include hemostasis, analgesic, and sedative. All the treatment should be given by intramuscular (IM) or intravenous (IV). Oral drugs should be avoided. Remember that this is only the initial treatment to help the patient feel better. Further treatment is required after full history and examination are performed and full diagnosis is made.

- **Step 3: Full history**
  - Details of the trauma:
    - How the trauma happened?
    - Which part of the body got hit (directly or indirectly)?
    - What hit the eye? The object's material, size, number, etc. (to see if possible IOBFs).
  - Medical history including current medication:
    - Health condition and medication before trauma.
    - What has been done since the trauma happened (any medical treatment or medications taken)?
  - History of allergy
  - Last meal and drink
  - Last tetanus shot
- **Step 4: Full ophthalmic examination**
  - Do not check IOP or put any pressure if there is concern for open globe.
  - BCVA.
  - RAPD.
  - Ocular motility and alignment.

- Slit lamp.
- Ophthalmoscope.
- IOP.
- Check if bleeding from the nose (sign of orbital medial wall fracture).

- **Step 5: Imaging**
  - Take a picture of the traumatic area.
  - CT scan is a noninvasive, noncontact, and quick examination. It helps on diagnosis of suspected IOFB or intraorbital foreign bodies, open globe, intraocular hemorrhage, orbital fractures, and many other cases. It is very useful and highly recommended in ocular trauma [3].
  - MRI is not recommended.
- **Step 6: Treatment**
  - In case of open globe:
    - Use Fox eye shield to prevent any pressure on the eyeball.
    - Antiemetics, antinauseants to prevent Valsalva.
    - Tetanus vaccine.
    - Antibiotics.
    - Blood test before surgery.
    - No food or drink if general anesthesia is needed.
  - Be prepared for surgery if needed:
    - Blood test.
    - Consent form.
    - Call OR for available time.
    - Call anesthesia for pre-op evaluation.
  - For treatment in detail, see Chap. 8.
  - Call senior doctor for help if there is any question.
- **Step 7: Admit or follow up** (Fig. 3.1)

3.2 Chemical Burn

- **Step 0: Before ophthalmologist**

Irrigate immediately with saline or with tap water if saline is not available

- **Step 1: Irrigation**
  - In chemical burn, irrigation is the most important step and should always be the first thing to do, even before VA test. The less duration of chemical contact with the eye, the better outcome.
  - Use normal saline or lactated Ringer's solution, 1–2 l, or irrigate for 10–15 min at least.
  - Use Morgan Lens if available.
  - Sweep to clean debris, evert the upper eyelid to clean fornices.
  - Irrigation until pH is normal.
- **Step 2:Examination**
  - The use of tropical anesthesia:
    - To relieve blepharospasm
    - To relieve pain for better examination under slit lamp
  - BCVA.
  - RAPD.
  - Slit lamp:
    - Pay special attention to epithelium defect and perilimbal ischemia.
  - IOP.
  - Check if there are burns on eyelids, face, or any other part of the body.
- **Step 3: History**
  - Patient can be wrong when describing the chemicals. It is recommended to ask patient to show pictures of the chemical bottle or bring the bottle if possible.
  - Medical history.
- **Step 4: Treatment** (see Chap. 9)
- **Step 5: Bandage contact lens**
- **Step 6: Admit or follow up** (Fig. 3.2)

3.3 Common Ocular Emergency

The most common chief complaints in ocular emergency are acute disturbance or loss of vision, acute pain, and red eye. They can be presented independently or, for the most of time, presented among each other. The key is to get full history and examination, make the right diagnosis, and start the treatment immediately in some extremely urgent diseases, such as CRAO, AACG, endophthalmitis, and so on [4]. A common patient care process listed below may help the medical staff to provide a quicker and better service for patients with such ocular emergency.

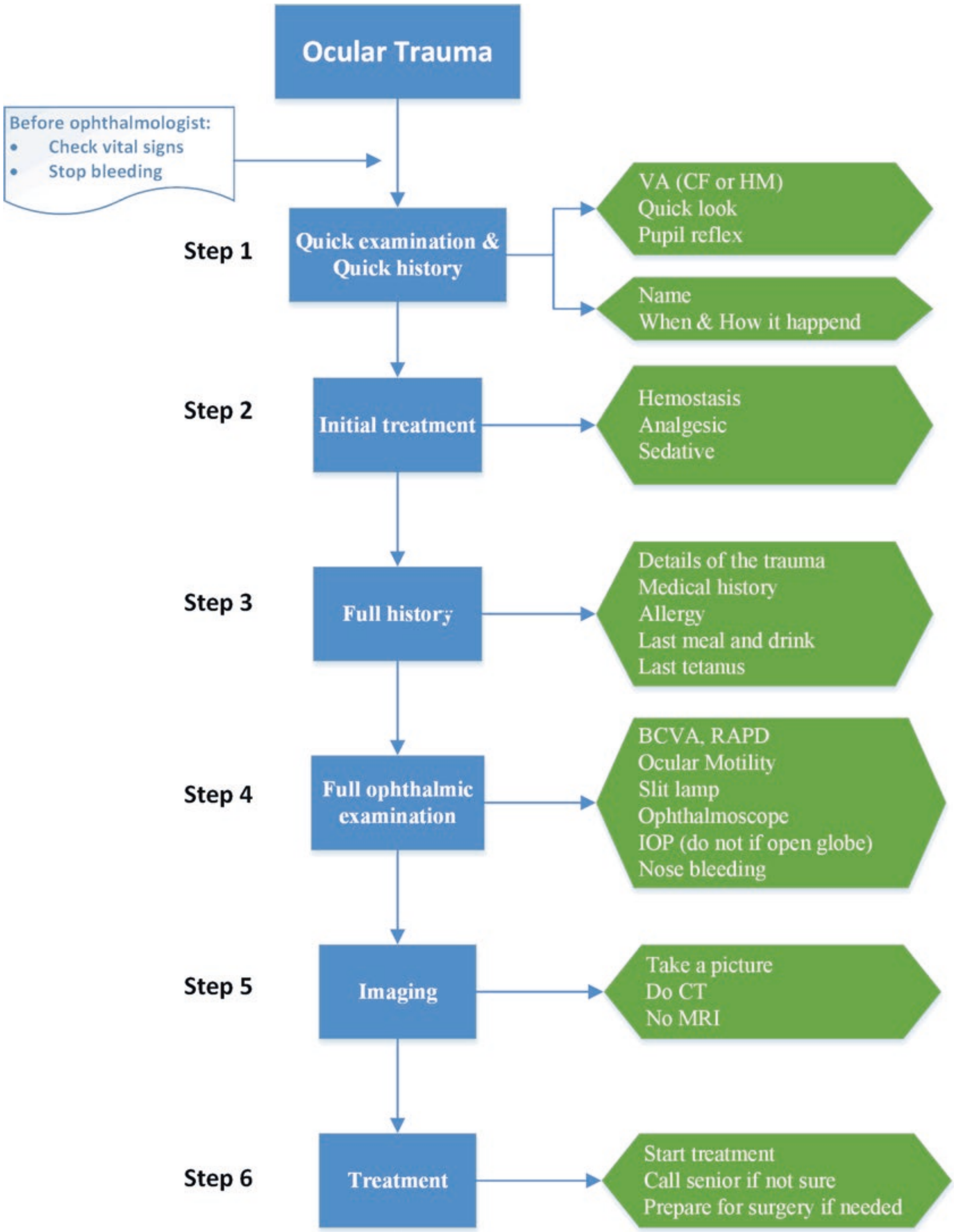

Fig. 3.1 Recommended patient care process of ocular trauma

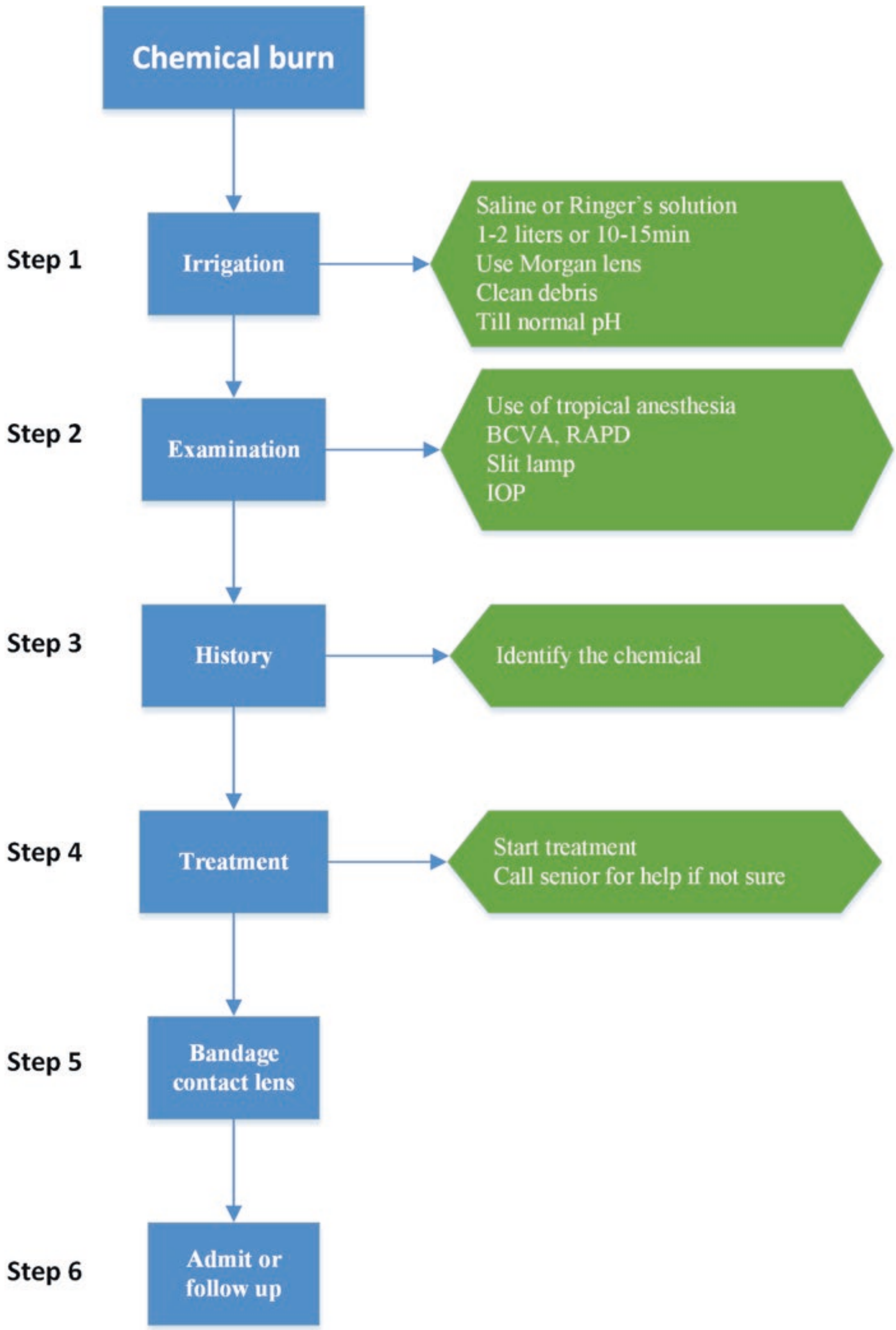

Fig. 3.2 Recommended patient care process of chemical burn

- **Step 0: Before ophthalmologist**
- Before ophthalmologist, blood pressure of the patient should be checked. Medication should be given for high blood pressure.
- **Step 1: Critical questions to ask**
  – Is there any pain/visual loss/red/discharge/itch/light sensitive in the eye?
  – When did it happen?
  – Happened before or first onset?
  – Better or worse over time?
- **Step 2: Full ophthalmic examination**
  – BCVA
  – RAPD
  – Ocular motility and alignment
  – Slit lamp
  – Ophthalmoscope
  – IOP
- **Step 3: Full history**
  – Transient visual loss (suggestive of amaurosis fugax)
  – History of sudden onset floaters and flashing light (suggestive of retinal detachment)
  – History of ocular trauma (suggestive of retinal detachment)
  – History of poorly controlled diabetes and laser treatment to the retina (suggestive of vitreous hemorrhage)
  – Headache +/jaw claudication in the elderly (suggestive of temporal arteritis)
  – Pain on eye movement in young patients (suggestive of optic neuritis)
  – History of glaucoma (suggestive of glaucoma attack)
  – History of hypertension, stroke, cardiac diseases, and carotid artery stenosis (suggestive of retinal artery occlusion) [5]
  – History of recent ocular surgery (suggestive of endophthalmitis, macular edema, VH, or RD)
  – Sudden binocular blindness with history of mental disorder, stress, or stimulate (suggestive of hysteria)
- **Step 4: Imaging**
  – B-ultrasound
  – OCT (in case of acute visual loss if available)
- **Step 5: Treatment**
  – Conditions need immediate treatment.
  – AACG.
  – CRAO.
  – Endophthalmitis.
  – For treatment in detail, see Chap. 8.
  – Call senior doctor for help if there is any question.
- **Step 6: Admit or follow up** (Fig. 3.3)

3.4 Mass Casualty

In situation of mass casualty, such as military combat, bombing, or tornadoes, significant ocular trauma accounts for about 8–25% of all injuries and is associated with over 30% of head injuries [6, 7]. There is no doubt that life is the highest priority in the chaos of mass casualty. However, eye injuries are generally underappreciated of the polyinjury spectrum, and the visual loss can make the survivors suffer even more than loss of limb amputation. In the rescue and emergency management, awareness and first response capabilities of ocular emergency should not lag [7, 8]. Ophthalmologist should be there, be a part of the lifesaving team, and be treating ocular trauma as close to the point of injury as possible. A recommended process will help the eye care medical staff provide quicker and better patient care, save time, and save sight. It should be noticed that every step of the recommended process is under the circumstances that life-threatening conditions are under control or the ophthalmic exam can be processed at the same time of lifesaving.

- **Step 0: Call backup early**
- In case of mass casualty, quick reaction and full preparation from the hospital are the key to saving lives. Medical staff should be updated of the event and have the firsthand information about the situation and the approximate number of casualties. Doctors and nurses are encouraged to stop the work with stable patient and participate in the mass casualty emergency if needed. Don't forget to call as many medical staff to come and help, even before the casualties arrive.

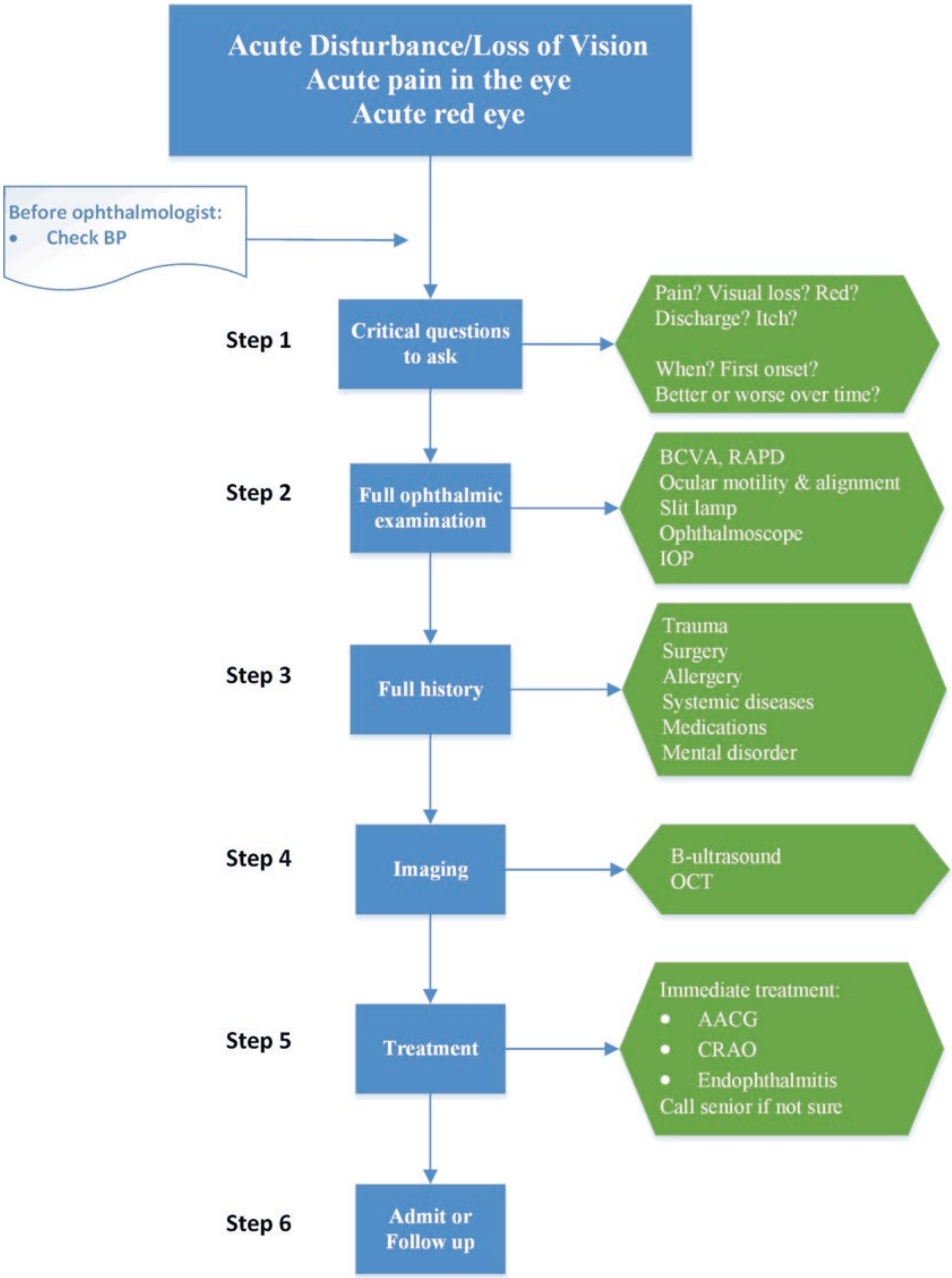

Fig. 3.3 Recommended patient care process of common ocular emergency

- **Step 1: Come prepared**
- In case of mass casualty, ophthalmologist is usually seeing a patient in the ER or on the floor; make sure you have stocked your bag properly for the exam you may need. It is recommended to have the listed equipment in the call bag:
  - Acuity card
  - Flashlight
  - Portable slit lamp
  - Ophthalmoscope (direct or indirect)
  - Tono-Pen
  - Fluorescein paper
  - Eye shields
  - Eye drops (topical anesthetics, tropicamide)
- – The call bag stocks may vary from hospital to hospital and it's fine. An ophthalmologist should always have a flashlight and a direct ophthalmoscope in the pocket for a go anytime, which are able to provide a quick exam and prioritization for the casualties.
- **Step 2: Triage**
- Every patient matters. However, in case of mass casualty, proper prioritization is necessary to save as many as possible. Triage is the process of determining the priority of patients' treatments based on the severity of their condition. Quick examination for triage should include VA and a quick look by flashlight. VA can be tested and recorded simply as CF (counting fingers), HM (hand motion), LP (light perception), or NLP (no light perception), just to give a quick appreciation of the level of damage to the eye. A quick and general diagnosis can be made by the VA, appearance, and pupil reflex. Based on the first impression, priority should be made as the following suggested order:
  1. Open globe and chemical burn: need immediate treatment.
  2. Optic nerve incarceration: needs urgent treatment and urgent surgery.
  3. Intraocular foreign bodies: need urgent treatment; surgery can wait after antibiotics and other treatments.
  4. Ocular contusion: treatment can wait in case of patient with higher priority present.
  5. Eyelid laceration: surgery can wait in case of patient with higher priority present.
- **Step 3: Patients assignment**
- When a patient was triaged of higher priority, he/she should be assigned to a group of medical staff who include at least one doctor and one nurse, who are in charge of the patient. Here we call it "two on one responsibility" which means two medical staff on one patient. They should respond mainly but not only on the patient's every step of treatment and medical care process below including transfer if needed.
- **Step 4: Transfer if necessary**
- In some cases, patients will need to be transferred to other hospital for the following reasons:
  - The number of casualties exceeds the capacity of hospital. In this case, the transferred patients should be stable and have relatively minor injuries.
  - The patient needs special surgery of which the doctors are not capable.
- **Step 5: Initial treatment**
- See the recommended patient care process for ocular trauma, step 2.
- **Step 6: Full diagnosis**
- Full diagnosis can be made by full history and ocular examination. For details, please see the recommended patient care process for ocular trauma, steps 3–5.
- **Step 7: Treatment**
- The general rule of treatment for mass casualty is to start treatment on high-priority casualties as soon as possible while keeping the other patients calm and stable. Surgery of mass casualty can be tricky. It may be performed in an OR not designed for ophthalmology, and the posture of patient may not be ideal for ocular surgery. Details should be well discussed with doctors from other departments to make an optimal surgical plan.
- **Step 8: Keep the relatives updated** (Fig. 3.4)

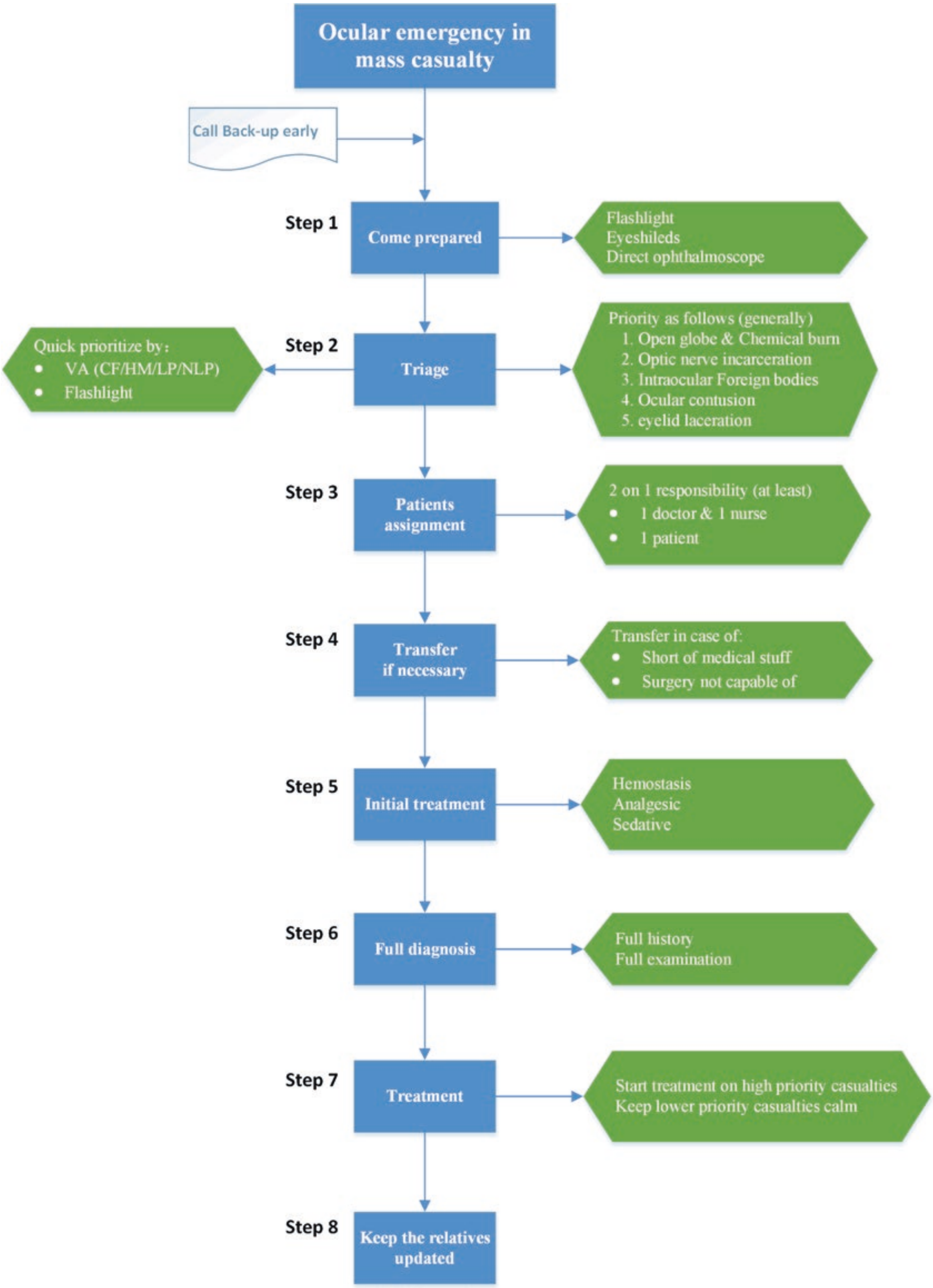

Fig. 3.4 Recommended patient care process of mass casualty

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4 Acute Redness of the Eye

Bo Huang

Abstract

Acute redness of the eye may involve the globe, lids, or adnexal structures. It is a very common clinical sign that is often associated with eye emergencies. The three major processes responsible for the majority of red eye cases are subconjunctival hemorrhages, ocular inflammation, and vascular abnormalities. Ocular inflammation accounts for the majority of red eye presentations, whereas vascular abnormalities are the least common causes. Successful diagnosis of red eye cases requires careful differential analysis of all the possibilities, careful examinations of medical and surgical history, and complete ophthalmic examinations. Major anterior segment etiologies associated with acute red eyes are discussed in this chapter.

Keywords

Red eyes · Conjunctivitis · Subconjunctival hemorrhage · Bacterial keratitis · Corneal abrasion · Corneal foreign body · Dacryocystitis

4.1 Overview

Acute redness of the eye is a very common and nonspecific sign. In general, a clinical sign of red eye indicates the visible appearance of abnormal redness of the globe, lids, or adnexal structures. The three major processes responsible for the majority of red eye cases are subconjunctival hemorrhages, ocular inflammation, and vascular abnormalities. Typically, ocular inflammation accounts for the majority of red eye presentations, whereas vascular abnormalities are the least common causes of red eyes. In some instances, two or all mechanisms can occur simultaneously.

Successful diagnosis of red eye cases requires careful differential analysis of all the possibilities, careful examinations of medical and surgical history, and complete ophthalmic examinations. The complete medical and ocular history should be acquired with the following essential components: the presence or absence of pain, the presence of accompanying symptoms such as foreign

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body sensation and itching, the presence and type of ocular discharge, photophobia, other visual disturbances, recent illnesses, and trauma. The complete eye examination must include visual acuity, pupil shape and reactivity, the gross appearance of the sclera and conjunctiva, extraocular muscle function, and palpation for preauricular nodes. The evaluation of the affected eye requires measurement of intraocular pressure, fluorescein staining, and a complete slit lamp evaluation and dilated fundus examination. In emergency situations, the clinician usually determines a number of probable diagnoses based on the initial history. A successful diagnosis would require additional historical and examination findings which either support the diagnosis or lead to other possibilities.

In this chapter, some of the major disease entities associated with the acute redness of the eye are discussed.

4.2 Subconjunctival Hemorrhage

Subconjunctival hemorrhage is a very common red eye case clinically. It is mainly caused by bleeding of the conjunctival or episcleral vessels deep to the conjunctiva into the subconjunctival space [1]. Subconjunctival hemorrhage can be spontaneous or related to trauma or systemic illness. Spontaneous subconjunctival hemorrhage is usually secondary to dry eyes with decreased lubrication of the eye [2]. The patient will usually present with a painless red eye with minimal decrease in vision. However, patients are often alarmed by the appearance when it first occurred. There is typically no discharge associated with subconjunctival hemorrhage. The patient may recall a history of mild trauma or Valsalva (such as coughing or vomiting). A history of anticoagulation therapy may also be elicited. Other medical history of hypertension, diabetes, or any bleeding disorder should be noted because subconjunctival hemorrhage may be a presenting sign of any of these conditions [3].

4.2.1 Ocular Manifestations

On examination, subconjunctival hemorrhage appears as well-defined area of fresh red blood on a white sclera. The hemorrhage typically masks the conjunctival vessels. When evaluating a subconjunctival hemorrhage, one should consider staining the cornea to rule out possibility of corneal injury if the patient has any type of pain associated with the subconjunctival hemorrhage (Fig. 4.1).

4.2.2 Treatment

If the subconjunctival hemorrhage is large and the patient presented in the setting of trauma, the possibility of penetrating injury to the globe (globe rupture) should be excluded with other diagnostic tests and in some cases may require emergency surgery for exploration. For minor subconjunctival hemorrhages, patient education and reassurance are the mainstays of treatment. Warm compress and frequent ocular lubrication drops may help reduce the symptoms and resolution of hemorrhage. Typically subconjunctival hemorrhage will take approximately 10–14 days to resolve [4].

Fig. 4.1 Subconjunctival hemorrhage. The blood deep to the conjunctiva has completely obscured the sclera underneath. The affected area has a slightly raised appearance

4.3 Conjunctivitis

Conjunctivitis may be infectious or noninfectious. The diagnosis is usually made clinically. If the diagnosis is not readily apparent, laboratory studies may be helpful in determining possible etiology.

4.3.1 Bacterial Conjunctivitis

Bacterial conjunctivitis is characterized by a rapid onset of unilateral conjunctival hyperemia, lid edema, and mucopurulent discharge. The second eye could become involved 1–2 days later.

The pathogenesis of bacterial conjunctivitis usually involves a disruption of the host defense mechanisms, e.g., abnormalities of the ocular surface secondary to eyelid abnormalities, tear film abnormalities, or systemic immunosuppression [5, 6].

Bacterial conjunctivitis can be classified into three clinical types: acute, hyperacute, and chronic (Table 4.1). The most common conjunctival pathogens include *Staphylococcus*, *Streptococcus pneumoniae*, *Haemophilus* species, *Moraxella*, *Corynebacterium diphtheriae*, *Neisseria* species, and enteric gram-negative rods [5].

Conjunctival membranes and pseudomembranes are among the findings associated with bacterial conjunctivitis and may be produced in association with *Neisseria gonorrhoeae*, β-hemolytic streptococci, and *C. diphtheriae*. Pseudomembranes, a combination of inflammatory cells and an exudate that contains mucus and proteins (Fig. 4.2), are loosely adherent to the underlying conjunctival epithelium and can be peeled away with no bleeding or damage to the epithelium. True membranes occur with more intense inflammation. The conjunctival epithelium becomes necrotic, and firmer adhesions are formed between the necrotic cells and the overlying coagulum. When the membrane is peeled, the epithelium tears to leave a raw, bleeding surface.

4.3.1.1 Acute Bacterial Conjunctivitis

Acute bacterial conjunctivitis usually begins unilaterally with hyperemia, irritation, tearing, mucopurulent discharge, and mattering of the lids (Fig. 4.3). Punctate epithelial keratitis can also occur. The most common pathogens include *Staphylococcus aureus*, *S. pneumoniae*, and *Haemophilus influenzae* [5]. The characteristic disease that results ranges from acute mucopurulent conjunctivitis to chronic, smoldering disease. Other common ocular manifestations include blepharitis, keratitis, marginal ulcers, and phlyctenulosis [7]. The pathogens *H. influenzae*, *S. pneumoniae*, *and Moraxella catarrhalis* occur more commonly in young children and may occur in institutional epidemics [8]. Often, *H. influenzae* is associated with systemic infection, including upper respiratory infection and fever.

The treatment of acute bacterial conjunctivitis consists of topical antibiotic drops or ointments. Although these infections are normally self-limited, lasting 7–10 days, antibiotic therapy usually speeds the resolution and lessens the severity of the disease. A broad-spectrum antibiotic with good gram-positive coverage such as a third- or fourth-generation fluoroquinolone, 10% sodium sulfacetamide, or trimethoprim-polymyxin may be used for 7–10 days.

4.3.1.2 Hyperacute Bacterial Conjunctivitis

The most common cause of hyperacute bacterial conjunctivitis is *N. gonorrhoeae* [5]. This oculogenital disease is seen primarily in neonates and sexually active young adults. Development of symptoms occurs within 24 h, and signs include profuse, thick, yellow-green purulent discharge,

Table 4.1 Pathogens that cause bacterial conjunctivitis

Acute	Hyperacute	Chronic
Staphylococcus aureus	*Neisseria gonorrhoeae*	*Staphylococcus aureus*
Streptococcus pneumoniae	*Neisseria meningitidis*	*Moraxella lacunata*
Haemophilus influenzae		*Enteric bacteria*

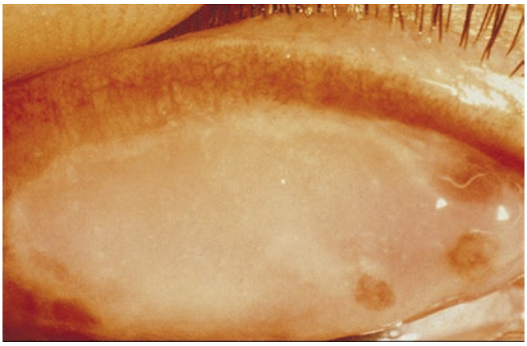

Fig. 4.2 Pseudomembrane. A combination of inflammatory cells, mucus, and protein exudate covers the superior tarsal conjunctiva

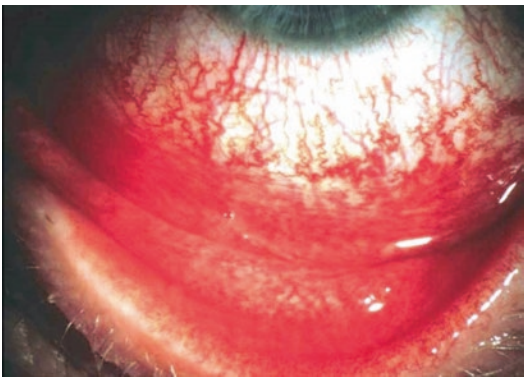

Fig. 4.3 Acute bacterial conjunctivitis. This patient was culture positive for pneumococcus

painful hyperemia, chemosis of the conjunctiva, and tender preauricular nodes. Untreated cases may lead to peripheral corneal ulceration and eventual perforation with possible endophthalmitis. A similar, but somewhat milder, form of conjunctival and corneal disease is caused by *Neisseria meningitidis.* Meningococcal conjunctivitis can be classified into primary and secondary. Primary meningococcal conjunctivitis can be either invasive (followed by systemic meningococcal disease) or noninvasive (isolated conjunctival infection) [9].

The treatment of hyperacute bacterial conjunctivitis is directed at the specific pathogen. Conjunctival scraping for gram stain and culture on blood and chocolate agar are strongly recommended. Gram-negative diplococci are suggestive of gonococcus. An effective regimen for gonococcal conjunctivitis includes 1 g of intramuscular ceftriaxone followed by a 2- to 3-week course of oral tetracycline or erythromycin. Topical medications may include penicillin (333,000 units/mL) or bacitracin or erythromycin ointment every 2 h. In meningococcal conjunctivitis, systemic treatment includes intravenous penicillin or, for penicillin-resistant infections, cefotaxime i.v. or ceftriaxone [9]. As large amounts of tenacious discharge occur, frequent irrigation of the ocular surface is helpful. Patients need to be seen daily to rule out corneal involvement.

4.3.1.3 Chronic Bacterial Conjunctivitis

Chronic bacterial conjunctivitis is defined by a duration of longer than 3 weeks. The most common causative organisms are *S. aureus* and *Moraxella lacunata*; others include the enteric bacteria *Proteus mirabilis*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Serratia marcescens* and *Branhamella catarrhalis* from the upper respiratory tract [5]. The most common causative agent in chronic bacterial blepharoconjunctivitis is *S. aureus*, which colonizes the eyelid margin, from which it causes direct infection of the conjunctiva or conjunctival inflammation through its elaboration of exotoxins [10]. Chronic angular blepharoconjunctivitis of the inner and outer canthal angles most commonly results from *M. lacunata*. A chronic follicular conjunctivitis may accompany both chronic angular blepharoconjunctivitis and chronic staphylococcal conjunctivitis.

The clinical signs of chronic staphylococcal conjunctivitis include diffuse conjunctival hyperemia with papillae or follicles, minimal mucopurulent discharge, and conjunctival thickening. Eyelid involvement may comprise redness, telangiectasis, lash loss, collarettes, recurrent hordeola, and ulcerations at the base of the cilia. Chronic staphylococcal blepharoconjunctivitis may lead to marginal corneal ulcers (Fig. 4.4). Maceration and crusting of the lateral canthal angle are seen in chronic angular blepharitis caused by *Moraxella* species.

The treatment of chronic bacterial conjunctivitis consists of proper antimicrobial therapy and

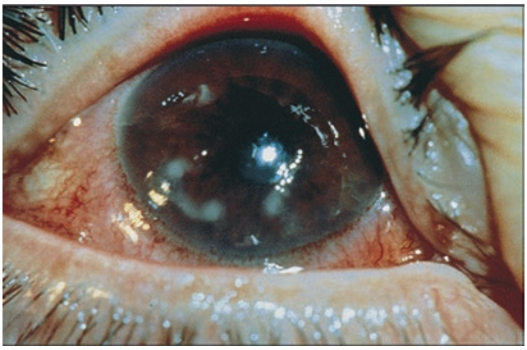

Fig. 4.4 Staphylococcal marginal keratitis. Note the inferior marginal corneal stromal infiltrates and the blepharoconjunctivitis

good lid hygiene, which includes hot compress and lid scrubs. Erythromycin and bacitracin ointments are commonly used topical antibiotics. When severe inflammation exists, antibiotic and corticosteroid combination drops or ointments can be used. Oral therapy with tetracycline 250 mg four times a day or doxycycline 100 mg twice a day or minocycline 50 mg twice a day may be needed for more severe infections.

4.3.2 Adenoviral Conjunctivitis

Viral conjunctivitis is extremely common. The diagnosis can usually be made clinically, so viral culture and laboratory investigation are rarely conducted [10]. Many different viruses cause conjunctivitis, and each produces a slightly different disease.

Adenoviruses produce the most common viral conjunctivitis with varying degrees of severity. These disease entities include follicular conjunctivitis, pharyngoconjunctival fever, and epidemic keratoconjunctivitis. Of the 41 adenovirus serotypes, 19 can cause conjunctivitis [11]. These infections are spread via respiratory droplets or direct contact from fingers to the lids and conjunctival surface. The incubation period is usually 5–12 days, and the clinical illness is present for 5–15 days [12]. After recovery, immunocompetent hosts are protected from further infection by the specific serotype that caused that infection.

4.3.2.1 Follicular Conjunctivitis

Follicular conjunctivitis is the mildest form of adenoviral conjunctivitis and is associated with adenovirus serotypes 1 through 11 and 19 [13]. It has an acute onset and is initially unilateral with possible involvement of the second eye within 1 week. It is manifested by a watery discharge and conjunctival hyperemia and is usually accompanied by follicular and papillary conjunctival changes and preauricular lymphadenopathy on the affected side. Most cases of viral conjunctivitis resolve spontaneously, without sequelae, within days to weeks.

4.3.2.2 Pharyngoconjunctival Fever

Pharyngoconjunctival fever is the most common ocular adenoviral infection [14] and is produced by adenovirus serotypes 3, 4, and 7. It is a condition characterized by a combination of pharyngitis, fever, and conjunctivitis. The conjunctivitis is predominantly follicular with a scant watery discharge, hyperemia, and mild chemosis. The cornea may be involved with a fine punctate epitheliopathy, and preauricular lymph nodes are enlarged in about 90% of cases. As the disease resolves spontaneously within 2 weeks, treatment is usually supportive with cold compress, artificial tears, and vasoconstrictor eye drops.

4.3.2.3 Epidemic Keratoconjunctivitis

Another common form of viral conjunctivitis is epidemic keratoconjunctivitis (EKC), produced by adenovirus serotypes 8, 19, and 37. It is a more severe type of conjunctivitis and typically lasts for 7–21 days. EKC produces a mixed papillary and follicular response of the conjunctival stroma with a watery discharge, hyperemia, chemosis, and ipsilateral preauricular lymphadenopathy (Fig. 4.5) [11, 15]. Subconjunctival hemorrhages, conjunctival membrane formation, and lid edema are common (Figs. 4.5 and 4.6) [13]. Membranes occur in approximately one third of cases and are more common with severe infections. Histologically, these conjunctival

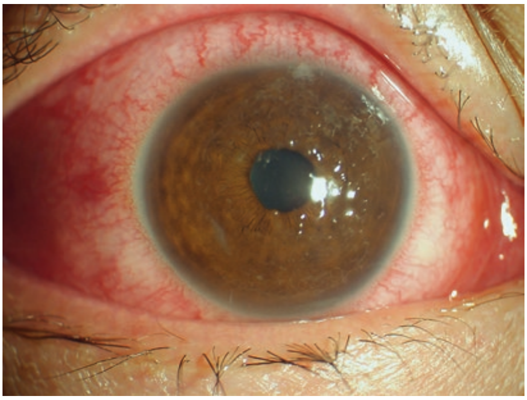

Fig. 4.5 Epidemic keratoconjunctivitis. (Thank professor Weiyun Shi for providing this picture.)

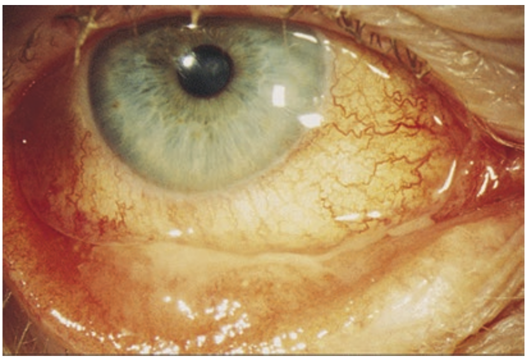

Fig. 4.6 Pseudomembrane in epidemic keratoconjunctivitis. An early pseudomembrane is forming in the inferior fornix

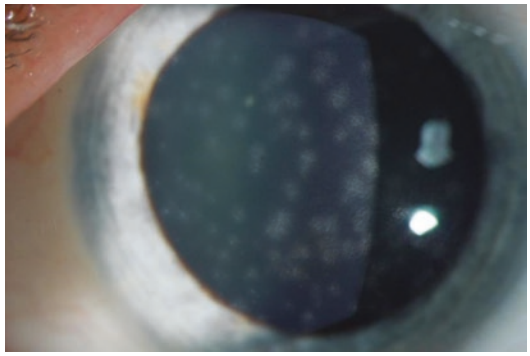

Fig. 4.7 Epidemic keratoconjunctivitis subepithelial infiltrates. These infiltrates develop 2 weeks after the onset of the disease and persist for months to years

membranes consist of fibrin and leukocytes with occasional fibroblast infiltration. Both true membranes and pseudomembranes may occur in EKC, and conjunctival scarring and symblepharon formation may occur after resolution.

Corneal involvement in EKC is variable. Most patients have a diffuse, fine, superficial keratitis within the first week of the disease. Focal superficial punctate epithelial lesions could develop by day 6–13 (Fig. 4.7), producing a foreign body sensation. By day 14, subepithelial opacities develop under the focal epithelial lesions in 20–50% of cases. Often, these opacities are visually disabling and may persist for months to years, but eventually they resolve with no scarring or vascularization [16].

Treatment of EKC consists of amelioration of symptoms and minimization of transmission of this highly contagious disease. Patients may be infectious for up to 14 days after onset [13, 17, 18], and outbreaks are especially common in ophthalmology offices and clinics. Transmission usually occurs from eye to fingers to eye, but tonometers, contact lenses, and eye drops are other routes of transmission. Preventive measures include frequent hand washing, relative isolation of infected individuals in an office setting, and disinfection of ophthalmic instruments [19, 20]. During the stage of acute conjunctivitis, treatment is usually supportive and includes cold compress and decongestant eye drops. When patients have decreased visual acuity or disabling photophobia from subepithelial opacities, topical corticosteroid therapy may be beneficial. High-dose topical corticosteroids, such as 1% prednisolone acetate three to four times a day, can help eliminate subepithelial infiltrates [21]. Cidofovir, an antiviral agent, has been investigated in the treatment of EKC [22, 23]. Although the application of cidofovir drops may prevent the formation of corneal opacities, its use has been limited by local toxicity and commercial unavailability.

4.3.2.4 Acute Hemorrhagic Conjunctivitis

Acute hemorrhagic conjunctivitis, also known as Apollo disease, was first described in Ghana during the time of the lunar landing mission of

1969 [24]. Two picornaviruses, enterovirus 70 and coxsackievirus A24, are the usual causative agents [25, 26] and, less commonly, adenovirus type 11. The signs of the disease include rapid onset of severe, painful follicular conjunctivitis with chemosis, tearing, lid edema, and the development of tiny subconjunctival hemorrhages. The hemorrhages are petechial at first and then coalesce, appearing posttraumatic. The cornea may be involved with a fine punctate keratopathy and, rarely, subepithelial opacities. The conjunctivitis resolves within 4–6 days, but the hemorrhages clear more slowly. The disease tends to occur in epidemics, especially in developing countries, with more than 50% of the local population affected in some cases. Very rarely, cases caused by enterovirus type 70 can result in a polio-like paralysis, which remains permanent in up to one third of affected individuals.

4.3.2.5 Herpes Simplex Conjunctivitis

Primary herpes simplex conjunctivitis usually occurs in children under 5 years of age. Most cases go undiscovered and undocumented because of their nonspecific nature. Typical signs include ocular irritation, watery discharge, mixed papillary and follicular conjunctivitis, hemorrhagic conjunctivitis, and preauricular lymphadenopathy [27]. Most cases are unilateral but may become bilateral. Epidermal vesicular eruptions of the eyelids and lid margins may accompany the conjunctivitis (Fig. 4.8), and the cornea may be involved. Corneal involvement may include a coarse, punctate epithelial keratitis, marginal infiltrates, or a dendritic ulcer. Although herpetic blepharoconjunctivitis is associated mainly with the primary disease, it may occur as a manifestation of recurrent disease with or without typical herpetic keratitis [27]. Most ocular herpetic infections result from herpes simplex virus type 1. Infections that result from the type 2 serotype may be seen in newborns or adults who have a history of oral-genital contact [28].

The conjunctivitis usually resolves spontaneously in 7–14 days without treatment [27]. Some physicians administer topical antiviral drops to patients with corneal involvement or to patients with lid vesicles with the goal of preventing corneal involvement. Corticosteroids in the treatment of patients who have acute follicular conjunctivitis should be closely monitored, as some of these patients may have herpetic disease and corticosteroids may enhance the severity of herpetic epithelial keratitis.

Fig. 4.8 Primary herpes simplex blepharoconjunctivitis. Note the bilateral vesicular eruptions in this child who has a primary herpes simplex infection

4.3.2.6 Other Causes

Other causes of viral conjunctivitis include the rubella, rubeola, varicella zoster, Epstein-Barr, and Newcastle disease viruses [25]. Rubella virus produces a nondescript, catarrhal conjunctivitis associated with the systemic disease, and a follicular reaction may occur. Rubeola produces a catarrhal, papillary conjunctivitis with tearing, pain, and photophobia. Pale, discrete, avascular spots, which resemble Koplik's spots seen in the mouth, may appear on the conjunctiva. Varicella zoster virus produces pustules and phlyctenule-like lesions on the conjunctiva, and a follicular conjunctivitis may occur with recurrent skin disease. Follicular conjunctivitis associated with the

Epstein-Barr virus occurs in association with infectious mononucleosis [29]. Newcastle disease viral conjunctivitis occurs in poultry workers and veterinarians in whom direct conjunctival inoculation of the virus has occurred while infected birds are handled [30]. The disease is self-limited, lasts 7–10 days, and leaves no ocular sequelae.

4.3.3 Chronic Follicular Conjunctivitis

Chronic follicular conjunctivitis is defined as the disease that lasts for more than 16 days [10]. *Chlamydia trachomatis*, an obligate intracellular bacterium, is the most common cause of chronic follicular conjunctivitis; the organism causes three clinical syndromes – trachoma, adult inclusion conjunctivitis, and neonatal conjunctivitis.

4.3.3.1 Trachoma

Trachoma, which results from *C. trachomatis* serotypes A–C, is endemic in many parts of the world and remains prevalent in Africa, the Middle East, Latin America, Central Asia, and Southeast Asia [31]. It is estimated that active trachoma affects about 150 million people worldwide, with about 10 million people developing secondary trichiasis and approximately 6 million case of blindness from sequelae of the disease. After an incubation period of 5–10 days, trachoma manifests as a mild mucopurulent conjunctivitis that is typically self-limiting and heals without permanent sequelae [32]. Repeated infections, however, result in chronic inflammation such as follicular conjunctivitis and papillary hypertrophy of the upper palpebral conjunctiva, a superior superficial corneal pannus, and fine epithelial keratitis. Multiple reinfection will eventually lead to scarring and cicatrization of the cornea, conjunctiva, and eyelids.

Complications of trachoma can cause severe loss of vision due to corneal ulceration and scarring secondary to severe conjunctival and eyelid scarring [33]. Cicatrization can result from the proliferation of connective tissue in the conjunctiva. Arlt's line (a horizontal line from conjunctival scarring at the junction of the anterior one third and posterior two thirds of the conjunctiva) is a characteristic finding on the superior pretarsal conjunctiva. Herbert's pits are a unique sequelae of trachoma [34]; these are sharply delineated depressions formed from necrosis and cicatrization of limbal follicles. A diffuse haze of the superior cornea can result after regression of the superior pannus. Eyelid abnormalities such as trichiasis, distichiasis, entropion, and ectropion may all occur. Other corneal complications, including scarring, vascularization, ulceration, and perforation, could all lead to decreased visual acuity and possible blindness.

Treatment of trachoma usually consists of a 3- to 4-week course of oral tetracycline (tetracycline 1 g/day or doxycycline 100 mg/day) or oral erythromycin. The clinical response may be slow and take 9–18 weeks. Therefore, topical tetracycline or erythromycin ointment is used twice a day for 5 days each month for 6 months [11]. Repeated topical therapy is especially useful where the disease is endemic and repeated exposure is likely. More recently, a single 20 mg/kg dose of oral azithromycin has been shown in several randomized controlled trials to be as effective as 6 weeks of topical tetracycline [32, 35–37]. Widespread use of systemic antibiotics in endemic areas has been tried in an attempt to eradicate the disease.

4.3.4 Adult Inclusion Conjunctivitis

Adult inclusion conjunctivitis results from *C. trachomatis* serotypes D–K. This chronic conjunctivitis presents as a unilateral red eye with mucopurulent discharge, marked hyperemia, papillary hypertrophy, and a predominant follicular conjunctivitis (Fig. 4.9). A tender, enlarged preauricular lymph node is common. Women often have a concomitant vaginal discharge secondary to a chronic cervicitis, and men may have urethritis. The conjunctivitis is often chronic in nature and often last many months. Keratitis may develop during the second week after onset of conjunctivitis. Corneal involvement includes a superficial punctate keratitis, small marginal or

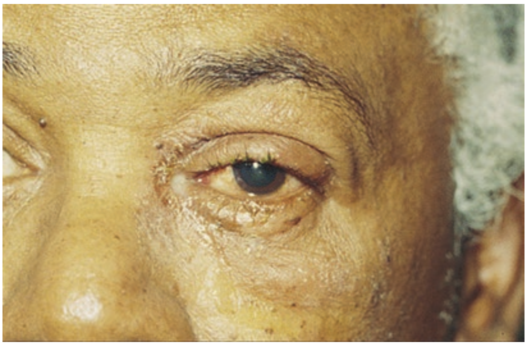

Fig. 4.9 Adult inclusion conjunctivitis. Prominent follicular conjunctivitis with a large and tender preauricular lymph node

central corneal stromal infiltrates, subepithelial infiltrates, limbal swelling, and a superior limbal pannus. If left untreated, keratitis and possible iritis can occur in the later stages of the disease.

Diagnosis is based upon the clinical appearance plus laboratory tests. Basophilic intracytoplasmic epithelial inclusions are seen with Giemsa staining of conjunctival scrapings. Immunofluorescent staining of the conjunctival scrapings is also useful. Serum immunoglobulin G (IgG) titers to chlamydia may be obtained.

The modes of disease transmission include orogenital activities and hand-to-eye spread of infective genital secretions. The incubation period is 4–12 days. It is estimated that 1 in 300 patients who have genital chlamydial disease develops adult inclusion conjunctivitis [38]. It is important to treat all sexual partners simultaneously to prevent reinfection. It also is prudent to rule out other venereal diseases, such as gonorrhea and syphilis. Treatment consists of systemic antibiotics, as topical antibiotics are relatively ineffective in the treatment of the eye disease. Treatments, which are given for 3 weeks, include oral tetracycline 500 mg four times a day, oral doxycycline 100 mg twice a day, or oral erythromycin stearate 500 mg four times a day. Tetracycline should be avoided in children younger than 7 years of age and in pregnant or lactating women. Recent studies suggest that a single 1 g dose of azithromycin is as effective as the standard therapies outlined above [39].

Table 4.2 Causes of neonatal conjunctivitis

Causes	Time of onset (postpartum)
Chemical (silver nitrate)	1–36 h
Chlamydia	5–14 days
Neisseria gonorrhoeae	24–48 h
Bacteria (*Staphylococcus*, *Streptococcus*, *Haemophilus*)	2–5 days
Virus (herpes simplex virus types 1 and 2)	3–15 days

The cause of the conjunctivitis is established by the clinical picture time course and laboratory confirmation

4.3.5 Neonatal Conjunctivitis (Ophthalmia Neonatorum)

Conjunctivitis of the newborn is defined as any conjunctivitis that occurs within the first 4 weeks of life (Table 4.2) [40]. It may be caused by a bacterial, viral, or chlamydial infection or by a toxic response to topically applied chemicals. Because the infectious agent may produce a severe localized infection of the eye plus a potentially serious systemic infection, precise identification of the cause is essential.

Some of the major risk factors for neonatal conjunctivitis include the following:

Organisms in the mother's birth canal
Maternal infections during pregnancy
Exposure of the infant to infectious organisms
Inadequate ocular prophylaxis immediately after birth
Susceptibility of the infant's eye to infection
Ocular trauma during delivery

Not all infants exposed to infectious agents in the birth canal develop conjunctivitis; the duration of the exposure is an important factor in the development of disease. Prevention still remains the best treatment as good prenatal care and treatment of chlamydial, gonococcal, or herpetic infections during pregnancy significantly lower the incidence of neonatal conjunctivitis. Proper eye cleaning using sterile cotton followed by the instillation of erythromycin or tetracycline antibiotic ointments immediately after birth helps prevent neonatal ocular infection. Studies have also suggested that instillation of 2.5% povidone-iodine as prophylaxis has superior bactericidal

effects and is also active against viruses, most notably herpes simplex [41].

4.3.5.1 Chemical Conjunctivitis

Chemical conjunctivitis classically results from the instillation of silver nitrate drops used for infection prophylaxis. The chemical conjunctivitis begins a few hours after delivery and lasts for 24–36 h. Approximately 90% of infants who receive silver nitrate develop mild, transient conjunctival injection with tearing [42]. The severity of these symptoms has been lessened since the development of single-use 1% buffered silver nitrate ampules. Although effective against *N. gonorrhoeae*, silver nitrate has a relatively limited spectrum of activity against other bacteria and is ineffective against chlamydial or viral infections [43]. Silver nitrate may be toxic to corneal epithelial cells and thus render the ocular surface more susceptible to invasion by other infectious agents. Although this method is still used in the majority of countries as the primary means of infection prophylaxis, many hospitals have switched to the use of less toxic agents such as erythromycin or tetracycline ointments.

4.3.5.2 Chlamydial Infections

The most frequent cause of neonatal conjunctivitis in the United States is *C. trachomatis*. Infants whose mothers have untreated chlamydial infections have a 30–40% chance of developing conjunctivitis and a 10–20% chance of developing pneumonia [44]. Symptoms typically develop 5–14 days after delivery and may be unilateral or bilateral. Initially, infants have a watery discharge that may progressively turn mucopurulent. Signs include lid edema, a papillary conjunctival response, and pseudomembrane formation (Fig. 4.10). Usually, the infection is mild and self-limited; however, severe cases may occur and result in conjunctival scarring and a peripheral corneal pannus with corneal scarring. If either erythromycin or tetracycline ointment is applied within 1 h of delivery, the chance of developing chlamydial conjunctivitis is markedly decreased [45].

Laboratory data are very helpful in the diagnosis of chlamydia. An enzyme-linked immunoassay test is nearly 90% sensitive and over 95% specific and provides results within several hours. A direct immunofluorescent monoclonal antibody stain of conjunctival smears is probably the most useful serological test as it has over 95% sensitivity and 77–90% specificity for chlamydia, depending on the prevalence of the disease. It may show infections missed by the other assays and can be read immediately. DNA detection techniques including polymerase chain reaction and ligase chain reaction are also available and are approximately 90% sensitive and 100% specific [46].

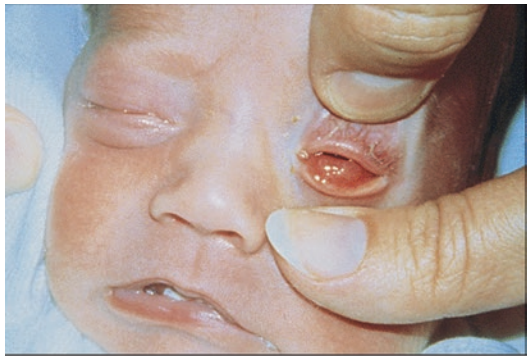

Fig. 4.10 A 10-day-old infant who has unilateral conjunctivitis. The mother had an untreated chlamydial infection of the birth canal

The objectives of the treatment of infants who have chlamydial conjunctivitis include the resolution of infectious conjunctivitis and the eradication of respiratory colonization. Topical therapy alone is not sufficient to treat chlamydial conjunctivitis. The recommended treatment is oral erythromycin syrup 50 mg/kg/day in four divided doses for 14 days. If a complete response does not occur, a second course of the same therapy may be given. The mother and sexual partners are treated with either oral tetracycline 500 mg four times a day or oral erythromycin 500 mg four times a day for 7 days [47] (pregnant or breastfeeding women are given erythromycin).

4.3.5.3 Neisserial Infections

Neonatal conjunctivitis is caused by *N. gonorrhoeae*, a gram-negative diplococcus that can penetrate an intact epithelium. The incidence of this disease has decreased significantly since the

advent of prophylaxis. The clinical manifestation of gonococcal conjunctivitis consists of the development of a hyperacute conjunctivitis 24–48 h after birth characterized by marked eyelid edema, profound chemosis, and excessive purulent discharge. The discharge is often so copious that it reaccumulates immediately after the eye has been wiped clean. Conjunctival membrane formation may occur. Because the organism may penetrate an intact epithelium, corneal ulceration with possible perforation can also occur if the conjunctivitis is not treated adequately [47].

Diagnosis is made by identification of gram-negative intracellular diplococci on smears from the conjunctiva. The organism is best cultured on chocolate agar or Thayer-Martin agar incubated at 37 °C in 10% carbon dioxide, and sensitivities should be obtained. Prompt diagnosis by examination of an immediate gram stain is essential to timely and effective therapy.

Local treatment consists of aqueous penicillin G 10000–20,000 units. Drops are given every hour with a loading dose of one drop every 5 min for 30 min. Systemic therapy should also be instituted with either intravenous aqueous penicillin G 100000 units/kg/day in four divided doses or penicillin G benzathine 50000 units/kg/day for 7 days. Intravenous or intramuscular ceftriaxone 25–50 mg/kg once a day for 7 days is also effective if there is suspicion of a penicillinase-producing strain.

4.3.5.4 Other Bacterial Infections

Many different organisms can cause bacterial neonatal conjunctivitis. Bacteria are probably transmitted through the air to the infant shortly after birth, and there may be an association with obstruction of the nasolacrimal duct. Usually, these infections are caused by gram-positive bacteria such as *S. aureus*, *S. pneumoniae*, *Str. viridans*, and *S. epidermidis*. Gram-negative organisms that have been implicated include *Haemophilus* species, *E. coli*, *Proteus* species, *K. pneumoniae*, *Enterobacter* species, and *Ser. marcescens* [48]. A rare cause, *Pseudomonas* sp., deserves particular mention in that infection with this organism can result in corneal ulceration and perforation [49].

Typically, these infections arise 2–5 days after birth but may occur at any time within the postpartum period. Signs include lid edema, chemosis, and conjunctival injection with discharge. The workup includes conjunctival scrapings for gram stain and cultures, the results of which direct the choice of therapy. For gram-positive organisms, erythromycin 0.5% ointment four times a day is administered. Gentamicin, tobramycin, or fluoroquinolone drops or ointment four times a day can be used for gram-negative organisms.

4.3.5.5 Viral Infections

Viral conjunctivitis of the newborn is rare but can be associated with significant morbidity and mortality. Both herpes simplex virus type 1 and herpes simplex type 2 can be associated with conjunctivitis, but type 2 infection is more common [50]. Type 1 may be transmitted by a kiss from an adult who has an active "cold sore," and type 2 is more commonly transmitted through the birth canal. Onset is usually within the first 2 weeks of life and may be associated with vesicular skin lesions of the lid or lid margin. The conjunctivitis may be followed by herpetic keratitis or keratouveitis. Vitritis, retinitis, retinal detachment, optic neuritis, and cataract have all been reported in association with neonatal ocular herpes. The diagnosis may be confirmed by the presence of eosinophilic intranuclear inclusions on smears, positive viral cultures, or positive monoclonal antibody immunoassays.

Treatment consists of trifluorothymidine 1% drops every 2 h for 7 days or acyclovir ointment five times a day. Herpes simplex type 2 may be more resistant to treatment. In cases of systemic disease associated with pneumonitis, septicemia, and meningitis, systemic acyclovir should be used. Good prenatal care and frequent culture and treatment of mothers who have known herpes genital infections decrease the incidence of herpetic neonatal conjunctivitis.

4.3.6 Fungal and Parasitic Conjunctivitis

Focal eyelid or conjunctival granulomas can be caused by rare infections including blastomycosis, sporotrichosis, rhinosporidiosis, *Cryptococcus*, leishmaniasis, and ophthalmomyiasis.

4.3.6.1 Microsporidial Keratoconjunctivitis

Microsporida are obligate, intracellular, spore-forming protozoan parasites that can cause disseminated disease or localized keratoconjunctivitis [51]. It is more commonly seen in immunocompromised patients but has been reported in immunocompetent patients especially associated with contact lens wear. Clinical symptoms include pain, redness, and, occasionally, visual blurring. Superficial, multifocal, coarse, punctate epithelial keratitis and a diffuse papillary conjunctivitis are typical of the disease [52]. Diagnosis is made with ocular surface scraping and visualization of acid-fast spores upon staining [53]. Electron microscopy can also be used to confirm and classify spores. Treatment includes topical fumagillin and oral albendazole [51].

4.3.6.2 Loiasis

Loa loa is a filarial nematode that is transmitted from human to human by the bite of an infected female deer fly (genus *Chrysops*) that is indigenous to West and Central Africa. The adult worm can migrate subcutaneously from the bite area to the eye. Skin manifestations as well as conjunctivitis can be present. Treatment consists of diethylcarbamazine 2 mg/kg t.i.d. for 3 weeks [53]. Ivermectin 150 mg/kg can also be used, but significant side effects include subconjunctival and retinal hemorrhages and cotton-wool spots [54].

4.3.6.3 Parinaud Oculoglandular Syndrome

Parinaud oculoglandular syndrome is an uncommon ocular complication of systemic *Bartonella henselae* infection (cat-scratch disease), affecting approximately 5–10% of patients [55]. *Bartonella henselae* are small, fastidious gram-negative rods that affect approximately 22,000 patients in the United States per year [56]. Ocular symptoms include unilateral redness, epiphora, foreign body sensation, and mild lid swelling. Serous discharge may be present; if an abscess forms and ruptures, purulent discharge can be noted. Granulomatous nodules develop on the palpebral and bulbar conjunctiva approximately 3 days after inoculation. Necrosis and ulceration of the overlying epithelium is common [37]. Firm and tender regional lymphadenopathy of the preauricular, submandibular, and, occasionally, cervical nodes is a hallmark of the disease. Optic neuroretinitis and multifocal chorioretinitis may develop. Diagnosis can be made by indirect immunofluorescence antibody testing or by enzyme immunoassay. Serologic testing includes cultures and polymerase chain reaction (PCR).

The course of the disease in immunocompetent patients is usually self-limited and resolves without antibiotic therapy. Therapy in immunocompromised patients is recommended. Currently recommended therapies include oral erythromycin, doxycycline, or azithromycin. In adults, doxycycline 100 mg twice daily is thought to be more effective due to its superior intraocular and central nervous system penetration. In more severe infections, these medications can be given intravenously, and rifampin can be used as an adjuvant [57].

4.3.7 Noninfectious Conjunctivitis

4.3.7.1 Amyloidosis

Amyloid is an avascular, noncollagenous protein that may be deposited in the conjunctiva, cornea, adnexal tissues, vitreous, retina, choroid, ciliary body, and orbit. Ocular involvement is most common in primary systemic or localized amyloidosis but may also occur as secondary localized amyloidosis associated with trichiasis, trachoma, chronic keratitis, keratoconus, and stromal corneal dystrophies [57]. Conjunctival amyloidosis is usually asymptomatic. It presents as a discrete, nontender, nonulcerative, waxy, yellow-white, firm subconjunctival mass. It is most often found in the inferior fornix but can occur anywhere on the bulbar conjunctiva or at the limbus (Fig. 4.11) [58].

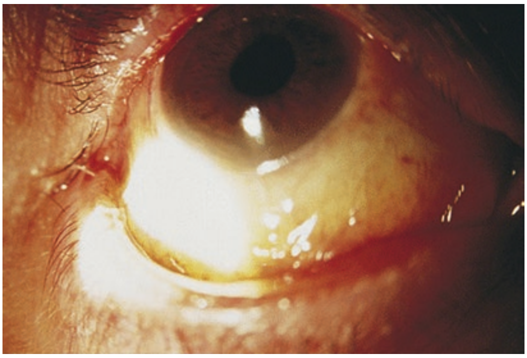

Fig. 4.11 Conjunctival amyloidosis associated with primary systemic amyloidosis

Fig. 4.12 Molluscum contagiosum lesion on the lower eyelid. This patient had an accompanying chronic follicular conjunctivitis secondary to the toxic effect of viral proteins from this lesion

Usually, the diagnosis is suspected on clinical grounds; however, definite diagnosis is made on the basis of biopsy. The histochemical reactions include birefringence and dichroism with Congo red, metachromasia with crystal violet, and fluorescence with thioflavin T.

Treatment may involve workup for systemic amyloidosis, but local excision of conjunctival masses is not usually necessary.

4.3.7.2 Toxic Follicular Conjunctivitis

Toxic follicular conjunctivitis follows chronic exposure of the conjunctiva to a variety of foreign substances, including molluscum contagiosum of the lid margin, infection of the lashes by *Pthirus pubis*, use of eye cosmetics, and prolonged use of various eye medications. Molluscum contagiosum infections are caused by a poxvirus and are common in the setting of human immunodeficiency virus infection. They are characterized by elevated, round, pearly white, waxy, noninflammatory lesions with umbilicated centers (Fig. 4.12). When these lesions occur on or near the eyelid margin, the viral proteins spill into the conjunctiva to cause a chronic follicular conjunctivitis [59]. The virus itself does not grow in the conjunctiva; rather the conjunctivitis is a toxic reaction to its proteins. Removal of the lesion or curettage until it bleeds internally eliminates this condition.

Most commonly, toxic follicular conjunctivitis occurs in association with eye medications, such as neomycin, gentamicin, idoxuridine, and other topical antivirals, as well as many glaucoma medications including brimonidine, pilocarpine, and other miotics. These drugs incite a type IV delayed hypersensitivity reaction with periocular erythema and a follicular conjunctivitis. In contact lens wearers, any proteolytic enzymes/chemicals used for contact lens cleaning or preservative-containing soaking solutions can cause toxic conjunctivitis. A marked follicular response can also accompany the use of eye cosmetics such as mascara and eyeliner. A common finding is dark granules from the cosmetic incorporated in the follicles. If symptomatic, patients usually respond well to discontinuation of the cosmetic and substitution of smaller amounts of hypoallergenic preparations.

4.3.7.3 Acute Allergic Conjunctivitis: Seasonal/Perennial

Acute atopic conjunctivitis is associated with a type I immediate hypersensitivity reaction. It is mediated by IgE and subsequent mast cell activation [60] stimulated by direct exposure of the ocular mucosal surfaces to environmental allergens such as dust, grass, molds, pollens, and spores. The reaction may be limited to the eye or may be part of a generalized allergic reaction with nasal and respiratory symptoms. Often, a family history of atopy is present. Cytological examination of conjunctival scrapings shows eosinophilic infiltration, and elevated levels of

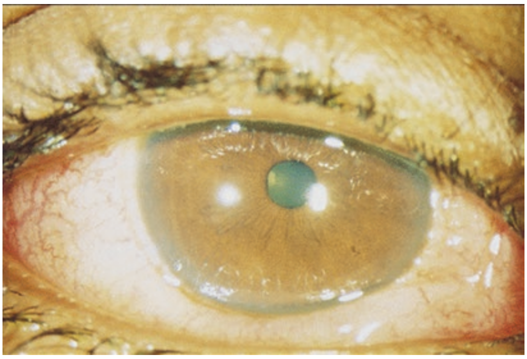

Fig. 4.13 Acute atopic conjunctivitis. A man with itching, mucoid discharge, chemosis, and a papillary conjunctival reaction

Fig. 4.14 Chronic atopic conjunctivitis. Mild conjunctival injection with numerous giant cobblestone papillae

IgE and histamine are found in the tear film [61]. Acute allergic conjunctivitis can be divided into two main categories: seasonal allergic conjunctivitis (SAC), which is more common, and perennial allergic conjunctivitis (PAC) [62]. The onset of symptoms for SAC is seasonally related to circulating antigens. PAC is considered a variant of SAC that persists throughout the year, although seasonal exacerbations are also often seen [61]. Clinical symptoms and signs are bilateral and consist of itching, burning, and mild to moderate injection that can progress to various degrees of glassy conjunctival chemosis with a papillary reaction of the superior tarsal conjunctiva. A watery or mucoid "stringy" discharge can also be seen (Fig. 4.13) [63].

4.3.7.4 Chronic Atopic Keratoconjunctivitis

Chronic atopic keratoconjunctivitis (AKC) is a chronic inflammatory disease that can lead to disabling symptoms involving both the conjunctiva and the cornea. It can present between the late teens through the fifth decade and has a slight male predominance. A large majority of patients have concomitant eczema or asthma [60]. Clinical symptoms include intense bilateral itching, tearing, burning, photophobia, blurred vision, and a stringy mucus discharge. Periorbital eczema, lid edema, conjunctival chemosis, and allergic shiners are common findings. Papillary hypertrophy of both upper and lower tarsal conjunctiva may occur and tends to be more prominent in the lower lid (Fig. 4.14). Gelatinous limbal hyperplasia and nodules may be present with or without Horner-Trantas dots (areas of eosinophils and degenerating cellular debris). In severe cases, cicatrizing conjunctivitis with subepithelial fibrosis, symblepharon formation, and forniceal shortening may develop [61]. Histopathologically, a mixture of mast cells, eosinophil, and lymphocytes is found in the conjunctival epithelium. The T cell is considered the primary effector cell in both chronic AKC and vernal keratoconjunctivitis [61, 62]. As this chronic condition also occurs in atopic individuals who have a compromised immune system, secondary infections must also be ruled out in these patients [64].

4.3.7.5 Vernal Conjunctivitis

Vernal conjunctivitis is a bilateral, recurrent inflammation of the conjunctiva that tends to occur in children and young adults with a history of seasonal allergy, asthma, or eczema. Its onset is most common in the spring and summer (hence the name vernal), and the inflammation often goes into remission during the cooler months [65]. The highest incidence of the disease is in the warm, temperate Middle East-Mediterranean region and Mexico. Boys are affected twice as often as girls with a peak incidence between the ages of 11 and 13 years. The disease is self-limited in children, with an average duration of 4–10 years. In adults, a more severe form of the disease may recur indefinitely. The prominent symptom is intense pruritis. Other complaints

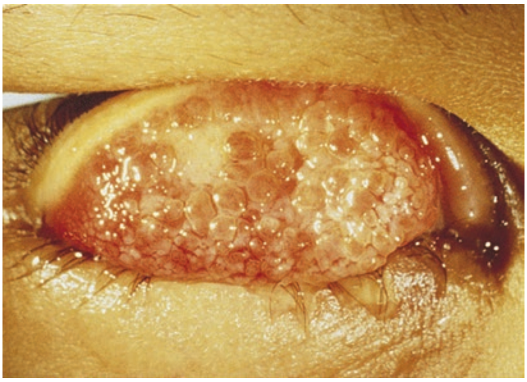

Fig. 4.15 Vernal conjunctivitis. Cobblestone papillae cover the superior tarsal conjunctiva

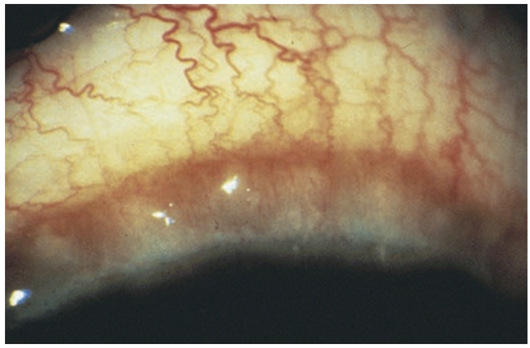

Fig. 4.16 Vernal catarrh. Clinical appearance of the less commonly seen limbal reaction

include photophobia, burning, tearing, mild ptosis, and a thick, ropy, yellow, mucoid discharge.

The three forms of the vernal conjunctivitis are palpebral, limbal, and mixed [66]. The palpebral form is marked by cobblestone papillae on the superior tarsal conjunctiva (Fig. 4.15), while the lower lid is minimally affected. There is initially papillary hypertrophy, after which the connective tissue of the substantia propria undergoes hyperplasia and proliferation to form giant papillae that can reach up to 7–8 mm in diameter. The pressure of the cornea flattens the tops of the giant papillae to produce a pattern that resembles cobblestones. Tiny twigs of vessels are found in the centers of the papillae, which helps to differentiate these from large follicles such as may be seen in trachoma. When wiped with a cotton-tipped applicator, a milky veil that overlies the cobblestones pulls off in a stringy fashion. The limbal form is marked by a broad, thickened, gelatinous opacification of the superior limbus that can override the cornea (Fig. 4.16). Again, tiny, twig-like vessels arise in the centers of these rounded lumps, whereas in limbal follicles, the vessels appear around the sides of the elevations. Histologically, the tissue is infiltrated with lymphocytes, plasma cells, macrophages, basophils, and many eosinophils. One of the typical characteristics of limbal vernal conjunctivitis is the presence of Horner-Trantas dots, which are white, chalk-like dots composed of eosinophils and epithelial debris located at the limbus.

The cornea can be involved in up to 50% of cases. Corneal manifestations include a superficial pannus and a punctate epithelial keratitis. Small, gray patches of necrotizing epithelium may involve the upper one third to two thirds of the cornea – in severe cases, the cornea appears to be dusted with flour [66]. The affected area stains with fluorescein. A vernal “shield ulcer” develops as a horizontally oval, shallow, nonvascularized, indolent ulcer of the superior cornea that leads to severe discomfort. The edges are composed of shaggy, gray, dead epithelial cells, and there is infiltration of the underlying superficial stroma. After the ulcer heals, a mild corneal opacity may persist at the level of Bowman’s layer.

4.3.8 Treatment of Allergic/Atopic Keratoconjunctivitis

Treatment of all of the above conditions is based on the severity and chronicity of the disease in each patient. For all cases, nonspecific measures can be used to help alleviate symptoms, including cold compress, preservative-free artificial tears (refrigerated), and avoidance of allergens. Unfortunately, avoidance of the offending antigens is often difficult. Medications then become necessary to control symptoms and any sequelae.

For moderate cases, treatment regimens include the use of topical decongestants, antihistamines, mast cell-stabilizing agents, and anti-inflammatory agents. Topical decongestants,

which act as vasoconstrictors, can be used symptomatically with mild allergic reactions to alleviate erythema and tearing. Rebound hyperemia with chronic use, however, limits their efficacy. Histamine (H_1 receptor-specific) antagonists such as levocabastine, azelastine, and emedastine difumarate can be used for acute allergic reactions from a short exposure to the antigen. Mast cell stabilizers such as cromolyn sodium, lodoxamide, pemirolast, and nedocromil sodium are used as long-term maintenance therapy for chronic allergies [67]. Combination medications that act as both mast cell stabilizers and H_1-specific antihistamines such as olopatadine, ketotifen fumarate, and azelastine have become a mainstay of treatment, and studies have shown the dual-mechanism medications to be effective in acute and chronic treatment [62]. Nonsteroidal anti-inflammatory agents can be used to reduce the acute inflammatory response until the mast cell stabilizers and antihistamines take effect.

In severe cases that are unresponsive to the medications outlined above, a short course of topical steroids is commonly used in addition to antihistamines and mast cell stabilizers in order to acutely control the inflammation. A good strategy by which to control the acute exacerbation of symptoms is to start with frequent topical corticosteroids combined with topical mast cell stabilizers or combination drops. The corticosteroids are then tapered off over a 2- to 3-week period as the therapeutic effects of the maintenance medications take hold. Topical ciclosporin 0.5–2% can be used if symptoms and inflammation persist. Researchers are currently investigating several other nonsteroidal immune modulators including topical tacrolimus, cytokine antagonists, and anti-IgE therapy [68–70]. Evaluation by an allergist is recommended in severe cases.

4.3.9 Allergic Dermatoconjunctivitis

Contact allergy of the eyelids and conjunctiva is the most common form of allergic reaction encountered by ophthalmologists. It represents a delayed, cell-mediated (type IV) hypersensitivity reaction. Previous sensitization can have occurred as little as 5 days or as long as years previously. The most common stimuli for this reaction are eye drops, cosmetics, clothing, jewelry, plastics, animal or vegetable products, and industrial chemicals [58]. The ocular drugs commonly associated with this reaction include neomycin, gentamicin, idoxuridine, atropine, thimerosal, and penicillin [71]. Other preservatives may stimulate allergy as well. The allergic reaction usually begins with severe itching and a papillary conjunctivitis that is worse on the inferior palpebral conjunctiva. A mucoid or mucopurulent discharge is seen. The adjacent skin of the lower lids and lateral canthi becomes involved in a typical eczematous dermatitis (Fig. 4.17). Chronic use of the allergen can lead to keratinization of the lid with eventual punctal edema and stenosis. The cornea may show punctate epithelial keratitis and erosions. Conjunctival scrapings show monocytes, polymorphonuclear neutrophil leukocytes, mucus, and eosinophils. Treatment consists of eliminating the antigenic stimulus and quieting the eye with antihistamines, mast-cell stabilizers, and topical corticosteroids.

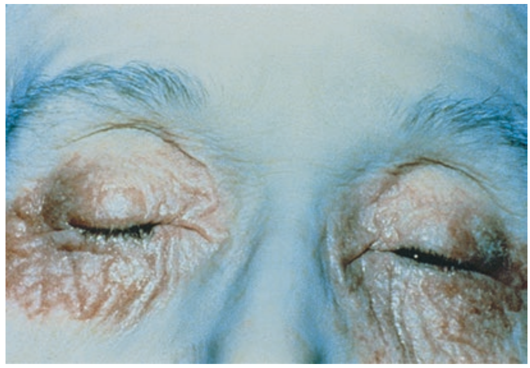

Fig. 4.17 Allergic dermatoconjunctivitis. Contact allergy of the eyelids after exposure to neomycin eye drops. The skin shows a typical eczematous dermatitis

4.3.10 Microbiallergic Conjunctivitis

Microbiallergic conjunctivitis is a type IV hypersensitivity response to the toxic protein breakdown products of bacterial disintegration. In the

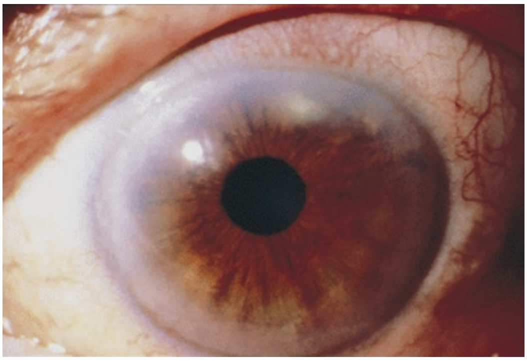

Fig. 4.18 Microbiallergic keratoconjunctivitis associated with staphylococci. A staphylococcal marginal infiltrate is seen in the superior cornea

eyes, the most common cause of this reaction is chronic staphylococcal blepharoconjunctivitis. This common infection results in the formation of breakdown products of the bacteria, which cause an allergic response in the conjunctiva and cornea [72]. Typically, patients do not have a history of atopy. Culture of the conjunctiva is negative for staphylococci. Marginal infiltrates of the cornea can be associated with this condition (Fig. 4.18) [58].

Phlyctenular keratoconjunctivitis is another manifestation of microbiallergic conjunctivitis. In the past, this condition was commonly associated with tuberculosis. Today, it is most frequently seen with chronic staphylococcal blepharoconjunctivitis. Other possible sources include *Candida albicans*, *Coccidioides immitis*, *Chlamydia*, parasites, and lymphogranuloma venereum. Phlyctenular disease presents as slightly raised, small, pinkish white or yellow nodules surrounded by dilated vessels located on conjunctiva near the limbus or on peripheral cornea. After a few days, the superficial part of the raised nodule becomes gray and soft; the center of the lesion then ulcerates, sloughs, and clears without scarring. Classically, there is no clear zone between the limbus and the lesion. Involvement is usually bilateral and seasonal (occurring more in spring and summer), and the condition occurs most frequently in children and young adults.

Treatment of these microbiallergic conjunctivitis requires an attempt to identify the inciting organism and eradicate it. In chronic staphylococcal disease, elimination of the inciting bacteria can be difficult. Twice-daily lid scrubs (mechanical debridement of the lid margins with dilute baby shampoo or commercially prepared lid scrub pads) can usually achieve symptomatic improvement. Topical antibiotic or antibiotic-corticosteroid combination ointments or drops rubbed into the lid margins may also reduce the number of bacterial colonies. Corticosteroids are reserved for chronic recalcitrant blepharoconjunctivitis and are beneficial early in the treatment of phlyctenular disease. Tuberculosis should be ruled out in children or young adults as well as any adult who has had a recently converted purified protein derivative skin test. Systemic antibiotics, such as oral tetracycline 250 mg four times a day or oral doxycycline 100 mg twice a day, can help in cases of nontuberculous phlyctenular disease or persistent staphylococcal blepharoconjunctivitis.

4.3.11 Giant Papillary Conjunctivitis

Giant papillary conjunctivitis (GPC) is a syndrome of inflammation of the upper palpebral conjunctiva associated with contact lens wear, ocular prostheses, and protruding ocular sutures [73, 74]. Primarily, this is a syndrome linked to contact lens wear and is seen ten times more frequently in soft lens wearers than in rigid lens wearers [74]. The average time for the development of symptoms is 8 months for soft lens wearers and 8 years for hard lens wearers. Estimates of the prevalence vary from 1% to 5% of soft lens users to 1% of rigid lens users.

The symptoms of GPC appear before the signs of superior tarsal involvement. Patients complain of mild itching after removal of the contact lenses and increased mucus on the lenses and in the nasal canthus upon awaking. They also complain of increased lens awareness, blurring of vision after hours of lens wear, excessive lens movement, and eventual contact lens intolerance. Signs of GPC initially include a generalized thickening and hyperemia of the superior pretarsal conjunctiva. The normally small papillae

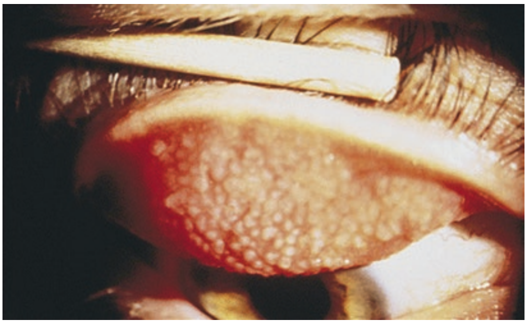

Fig. 4.19 Giant papillary conjunctivitis. Giant papillae cover this patient's superior tarsal conjunctiva after chronic exposure to soft contact lenses

become elevated. The conjunctiva becomes more translucent and eventually becomes opaque secondary to cellular infiltration. Macropapillae (0.3–1.0 mm) and giant papillae (1.0–2.0 mm) then form (Fig. 4.19). Trantas dots and gelatinous nodules may develop at the limbus [75]. Inspection of the contact lenses almost always reveals whitish deposits.

The histology of GPC shows irregular thickening of the conjunctival epithelium over the papillae, with epithelial downgrowth into the stroma. The epithelium and stroma show infiltration of lymphocytes, plasma cells, polymorphonuclear neutrophil leukocytes, eosinophils, basophils, and macrophages along with fibroblast proliferation. The number of eosinophils and basophils is considerably lower than that seen in vernal conjunctivitis.

The cause of GPC is multifactorial. Patients are likely to have environmental antigens adhere to the mucus and proteins that normally coat the surface of all contact lenses [76]. These antigens, which persist as deposits on the contact lenses, are forced into repeated contact with the superior tarsal conjunctiva with blinking. Mechanical trauma to the conjunctiva is also an important factor in the pathogenesis of GPC and develops in patients who have ocular prostheses and exposed sutures. The repeated exposure to antigen combined with the trauma to the upper tarsal conjunctiva from contact lens wear may trigger a type IV basophil hypersensitivity of the conjunctiva, which resembles cutaneous basophil hypersensitivity. A type I IgE-mediated immediate hypersensitivity reaction occurs as well. Conditions that favor the development of GPC in lens wearers include increased lens deposits, increased wearing time, extended number of years the lenses have been worn, larger diameter lenses, and soft lenses.

Treatment of the condition requires removal of the inciting factor. Loose sutures should be removed and ocular prostheses may need to be refitted. In contact lens wearers, initial discontinuation of lens wear is necessary until the inflammation subsides. Lens wear may resume once symptoms improve, but decreasing daily wear time and good lens hygiene are essential. Patients must be instructed to clean their contacts thoroughly each night, and an attempt should be made to remove preservatives from the lens care system. Disinfection with a hydrogen peroxide system and regular enzymatic treatment help decrease buildup on the lenses. Initially, a new lens of the same design may be used, but if this is not tolerated, a different lens design should be substituted. Two-week or daily disposable soft contact lenses should be encouraged and are often well tolerated. If soft lenses do not work, a rigid gas-permeable lens can be tried. When used in the early stages of GPC, a combination drop of antihistamine and mast cell stabilizer can be effective in the resolution of symptoms such as mucus production and itching. Maintenance therapy with combination drops or just mast cell stabilizers is typically necessary to prevent recurrence. A short course of topical corticosteroids can lessen the symptoms in severe cases.

4.4 Bacterial Keratitis

Bacterial keratitis often presents as an ocular emergency. It is caused by the proliferation of microorganisms and the associated inflammation and tissue destruction on cornea tissue. Bacterial keratitis rarely occurs in the normal eye because of the human cornea's natural resistance to infection. However, predisposing factors including contact lens wear, trauma, corneal surgery, ocular surface disease, systemic diseases, and immunosuppression may alter the defense mechanisms of

the ocular surface and permit bacteria to invade the cornea. Bacterial keratitis can be caused by multiple microorganisms. *Staphylococci* and *Pseudomonas* are the most common organisms in the United States. In contrast, streptococci, particularly *Streptococcus pneumoniae*, are a predominant cause of bacterial keratitis in many developing nations [77].

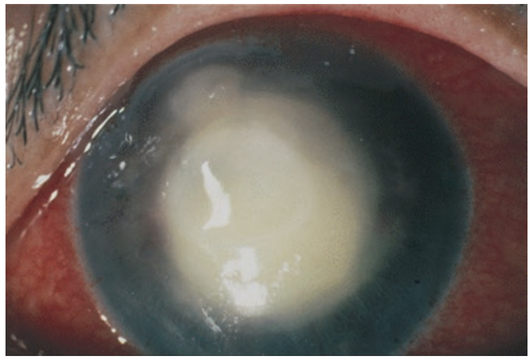

Fig. 4.20 Bacterial corneal infection with dense central necrotic ulcer and infiltrate

4.4.1 Ocular Manifestations

The clinical signs and symptoms of microbial keratitis can be variable depending on different factors which include the virulence of the organism, duration of infection, preexisting corneal conditions, immune status of the host, and previous use of antibiotics or corticosteroids. Clinically bacterial keratitis usually has a history of rapid onset of pain, photophobia, decreased vision, conjunctival injection, anterior chamber reaction, and/or hypopyon. Ultimately, gram stain and culture are required to distinguish the causing organisms. However, clinical diagnosis is possible when a pertinent history is available or the organisms present with characteristic features, such as a rapidly progressive stromal necrosis with mucopurulent discharge in *Pseudomonas aeruginosa* keratitis in a young patient with extended contact lens wear. In some cases, microorganisms such as fungi or *Acanthamoeba* can cause masquerading syndromes mimicking bacterial keratitis. The purpose of clinical evaluation of bacterial keratitis is to evaluate predisposing or aggravating factors in order to arrive at a differential diagnosis, to assess the severity of the disease and the associated complications, and to initiate appropriate management in a timely manner.

Patients may describe decreased vision, pain, and photophobia. The cardinal corneal sign is a localized or diffuse infiltration of the epithelium or stroma (Fig. 4.20). Commonly, there is epithelial absence over a gray-white necrotic stromal infiltrate. Alternatively, a stromal abscess can appear beneath an intact epithelium. Infiltration and edema of the cornea can appear distant to the primary site of infection. Occasionally, bacterial keratitis can present with predominantly multifocal epithelial infiltration, especially in the setting of hydrophilic contact lens wear.

Other ocular structures usually demonstrate associated inflammation. There is often some degree of lid erythema and edema, conjunctival injection and chemosis, tearing, and discharge. A nonspecific conjunctival papillary response might be seen. Anterior chamber inflammation is often present, with cells and flare. The inflammatory response might be so severe as to produce a hypopyon, but in the absence of a full-thickness corneal perforation, this most often represents a sterile accumulation. The aqueous might become dense and fibrinoid, and fibrinous endothelial plaques might develop.

4.4.2 Diagnosis

The presumptive diagnosis of infectious keratitis is based primarily on the clinical history and physical examination, but confirmation of infectious infiltration and definitive identification of the offending organism can be achieved only by examining stained smears of corneal scrapings and laboratory cultures of these scrapings. In practice, specific identification of the offending organism and antibiotic sensitivity data are necessary to guide the modification of antibiotic treatment if the initial antibiotic regimen fails. Since approximately 95% of suspected bacterial ulcers respond favorably to a well-chosen initial

antibiotic regime [78, 79] treatment modification is rarely necessary. Many practitioners therefore defer diagnostic stains and cultures for selected cases of suspected bacterial keratitis. There is some evidence, however, that small infiltrates that are not associated with advanced suppuration or severe intraocular inflammation respond favorably to this approach [79]. There is no debate that scrapings are mandatory if the infection is advanced or central or if the patient's history or the appearance of the infection is at all suggestive of filamentous bacterial, nontuberculous mycobacterial, gonococcal, mycotic, or protozoal infection.

When scrapings of corneal ulcers are obtained, material should be taken from the most active regions. The eye is anesthetized with topical anesthetic, and a heat-sterilized platinum spatula or blade is used to firmly scrape the leading edges of the ulcer. Multiple areas of a large ulcer should be sampled. If significant corneal thinning is evident, care must be exercised not to precipitate perforation. Some investigators have reported acceptable organism recovery rates with scrapings performed with a calcium alginate swab moistened with soy broth [80]. Scrapings should be placed on a slide for staining and directly applied to culture media, such as plates and broth, to maximize the chance of recovery. The commonly used culture media are described in Table 4.3. Multiple C streaks should be used on agar plates, because it is often difficult to identify an organism recovered in culture as the offending pathogen and growth outside of the C streak might indicate contamination.

The most commonly applied stains are gram and Giemsa stains (Table 4.4). Gram stain is useful to identify bacteria and yeasts, and Giemsa stain is useful for cytology and to identify bacteria (all stain blue), fungi, and chlamydia inclusions. If filamentous bacterial or nontuberculous mycobacterial infection is suspected, a Ziehl-Neelsen stain should be performed.

Corneal biopsy is indicated when an apparent infection fails to resolve in spite of antimicrobial treatment, the identity of the organism is in doubt, and conventional scrapings have failed to demonstrate a reasonably culpable organism [81].

Table 4.3 Common culture media

Medium	Organism	Comment
Blood agar	Aerobic bacteria	37 °C for bacteria
	Saprophytic fungi	Room temperature for fungi
Chocolate agar	*Haemophilus*, *Neisseria*, *Moraxella*	5–10% CO_2
Brain-heart infusion (BHI)	Bacteria	
	Fungi	
Sabouraud dextrose agar	Fungi	Room temperature
Enriched thioglycollate broth	Aerobic and anaerobic bacteria	Good for small inocula
Löwenstein-Jensen agar	Nontuberculous mycobacteria	
Escherichia coli-plated nonnutrient agar	*Acanthamoeba*	Transport sample to plate in page saline

Table 4.4 Stains for smears and corneal scrapings

Stain	Organism	Comment
Gram	Bacteria, fungi, *Acanthamoeba*, microsporidia	Stains walls of fungi
Giemsa	Bacteria, fungi, chlamydial inclusions, *Acanthamoeba*, microsporidia	All stain blue; does not demonstrate intranuclear inclusions; stains fungal cytoplasm
Gomori's methenamine silver	Fungi	Difficult technique
Ink-potassium hydroxide	Fungi	Displays fungal walls
Periodic acid-Schiff (PAS)	Fungi	
Acridine orange	Bacteria, fungi, *Acanthamoeba*	Requires fluorescent microscope
Calcofluor white	Fungi, *Acanthamoeba*	Requires fluorescent microscope
Weber	Microsporidia	
Ziehl-Neelsen	Mycobacteria, *Nocardia*, *Actinomyces*	

Corneal stromal biopsy is sometimes necessary to identify protozoan, mycobacterial, or mycotic organisms. As with corneal scrapings, the corneal biopsy specimen should incorporate the active edge and base of the ulcer. If the infiltrate is sequestered within the stroma, a lamellar technique is required. Tissue obtained by biopsy should be sectioned, with a portion submitted to the pathologist for microscopic examination, and a portion used for direct inoculation of plates and broth for microbial culture and antibiotic sensitivity studies.

4.4.3 Treatment

Topical broad-spectrum antibiotics are used initially in the empirical treatment of bacterial keratitis. For central or severe keratitis, initially a loading dose every 5–15 min is administered for the first hour, followed by applications every 15 min–1 h around the clock to achieve a sustained therapeutic level. For less severe keratitis, a less frequent dosing is appropriate depending on the clinical scenario. Cycloplegic agents may be used to prevent synechia formation and to decrease pain and ciliary spasm in more severe cases. Single-drug therapy using a fluoroquinolone (e.g., third or fourth generation) has been shown to be as effective as combination therapy utilizing fortified antibiotics. Some pathogens (e.g., *streptococci*, anaerobes) reportedly have variable susceptibility to fluoroquinolones, and the prevalence of resistance to fluoroquinolones appears to be increasing. For small and peripheral ulcers, it is generally acceptable to initiate treatment without performing corneal cultures.

Broad-spectrum antibiotics, either fortified or commercial preparations, are chosen based on the preexisting community data. For central, large, and deep ulcers, the antibiotic should be chosen based on the microbiological information.

4.5 Corneal Abrasions

Corneal abrasions are one of the most common ophthalmic injuries encountered in the emergency room. The common causative agents of corneal abrasion include fingernails, paper, mascara brushes, and plants. Important noncontact sources of epithelial injury include chemicals, radiation, and heat.

4.5.1 Ocular Manifestations

The most common symptoms of corneal abrasion are pain, photophobia, foreign body sensation, tearing, and decreased vision. The slit lamp examination of cornea can reveal areas of epithelial defects, which can be confirmed with the application of fluorescein dye. When illuminated with a light source through a cobalt blue filter, the dye will stain the defect apple green. When examining a patient with a corneal abrasion, the examiner should be alert to the possibility of other more serious ocular injuries, such as globe perforation. It is not uncommon for a high-velocity, sharp-edged foreign body to pass completely through the cornea with only clinical signs of corneal epithelial defect.

4.5.1.1 Treatment

Treatment of corneal abrasion usually includes the instillation of a cycloplegic agent and topical antibiotics. Because pain is a major complaint in patients with corneal abrasions, pain control is a significant issue. However, under no circumstances should a topical anesthetic be prescribed for the patient. With prolonged use of the topical anesthetics, corneal sensation and immune function are compromised, and severe sight-threatening complications may result. Most corneal abrasions heal spontaneously without difficulty in 24–48 h and without scarring if Bowman’s membrane is uninvolved.

4.6 Corneal Foreign Body

Corneal foreign bodies are frequently encountered ophthalmic trauma. The use of protective eyewear is crucial in preventing these injuries. Most corneal foreign body injuries, however, are not severe and do not result in prolonged morbidity if treated timely.

4.6.1 Ocular Manifestations

When a foreign body injury is suspected, the examiner should rule out the possibility of intraocular foreign body. A careful ocular injury history and a complete eye exam along with diagnostic tools such as gonioscopy, indirect ophthalmoscopy, ultrasound, and computed tomography (CT) scanning can be used to make the proper diagnosis. Most corneal foreign bodies are visible by careful slit lamp examination, although the findings may be subtle.

The slit lamp evaluation in the setting of foreign body injury should be thorough and meticulous. The examiner should look for possibility of multiple foreign bodies. Use of various illumination techniques is helpful. The application of fluorescein to cornea may also be of assistance with identifying smaller foreign bodies. Care should be taken to determine the depth of the material in the stroma using high magnification and narrow slit width, since this will assist with the decision for and technique of subsequent removal.

4.6.2 Treatment

Foreign bodies located on the surface can be removed using various approaches. For foreign bodies located in the superficial cornea, gentle application of a cotton swab may be sufficient. For more adherent and deeper foreign body, a tuberculin syringe with an attached 27- or 30-gauge needle is an effective instrument for removal. The needle is small enough to delicately remove even minute particles, and the barrel of the syringe provides a comfortable grip for easy maneuver.

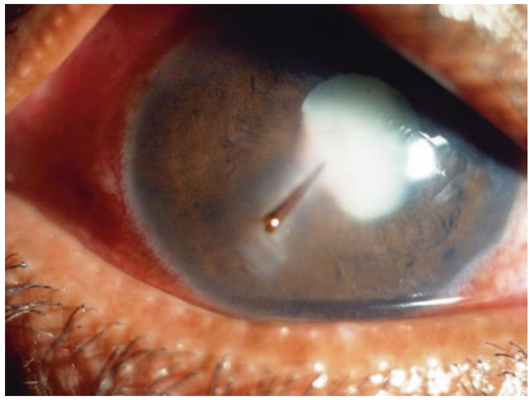

Fig. 4.21 Corneal foreign body

Ferrous foreign bodies pose a special problem of rust ring when embedded in the cornea. Rusting begins almost immediately after the object is embedded, and a ring may begin to form as early as 3 h after injury. The presence of the rust in the tissue not only interferes with vision but is also toxic to the cornea and retard healing. Rust rings need to be removed either by scraping with a small needle or by the application of a rotating burr to the involved area. After removal of the foreign body, the eye should be treated with the application of a broad-spectrum antibiotic and a cycloplegic agent (Fig. 4.21).

4.7 Dacryocystitis

Dacryocystitis can be acute, subacute, or chronic. It may be localized in the sac, extend to include a pericystitis, or progress to orbital cellulitis. When dacryocystitis is localized to the sac, a palpable painful mass occurs at the inner canthus (Fig. 4.22), and obstruction is present at the junction of the nasolacrimal sac and duct. A preexisting dacryocystocele may or may not be present. Approximately 40% of acute dacryocystitis does not recur, but in the rest of the cases, repeated attacks occur. Chronic dacryocystitis may be the end stage of acute or subacute dacryocystitis, and it may also present initially as a subclinically infectious cause of nasolacrimal duct obstruction. *Staphylococcus aureus* is the most common causative organism for dacryocystitis.

Fig. 4.22 A patient who has dacryocystitis localized to the lacrimal sac. Mild pericystitis exists

Fig. 4.23 A patient who has dacryocystitis and orbital cellulitis. Ocular mobility is limited, indicating infection posterior to the orbital septum

In dacryocystitis with pericystitis, there is percolation of infected debris through the mucosal lining of the wall of the sac, and infection around the sac is present. The infection may spread to the anterior orbit and produce a tremendous amount of eyelid swelling (Fig. 4.23). If the infection proceeds posterior to the orbital septum, as might occur in immunocompromised patients, a true orbital cellulitis may occur, resulting in globe proptosis or displacement, afferent pupillary defect, motility disturbance, optic neuropathy, and even blindness.

4.7.1 Treatment of Lacrimal Sac and Duct Obstruction

4.7.1.1 Congenital Nasolacrimal Obstruction

More than 90% of patients with congenital nasolacrimal obstruction undergo spontaneous resolution by 1 year of age [82]. Therefore, initial probing should be postponed until this age.

The probe is usually achieved by entering the lower canaliculus with the lid stretched laterally. The probe is turned past the 90° angulation and advanced inferiorly until it perforates the membrane. Fluorescein-tinted irrigation saline is introduced to see whether it passes into the inferior meatus, and metal-to-metal contact may be obtained by inserting a probe into the nose. The success rate of probing is greater than 90%.

If the repeat probing does not proceed easily, Silastic tubes should be placed and left for at least 3 months (preferably 6 months). If these tubes fail and the child is still symptomatic, a DCR procedure can be considered.

4.7.1.2 Acquired Nasolacrimal Obstruction

After an attack of dacryocystitis or obstruction, patients can be observed because some symptoms may resolve spontaneously. Medication such as naphazoline nasal spray shrinks the nasal mucosa and may be used for a short for symptomatic relief.

Medications such as antihistamines, either topical or local, and botulinum toxin have been reported to decrease lacrimal secretion. Surgical removal of the palpebral lobe of the lacrimal gland has been attempted, but there is a risk of producing a dry eye.

In the presence of frank dacryocystitis, it is important to treat the infection. If orbital cellulitis is suspected, a CT scan is obtained to rule out an abscess, and intravenous antibiotics are used. If the infection does not resolve and perforation is impending, a dacryocystotomy should be

performed. After injecting lidocaine (lignocaine), an incision is made directly over the lacrimal sac, and the debris within the sac is curetted. Transcutaneous aspiration of sac contents for culture may be done with a No. 22 needle.

If epiphora persists after resolution of the infection, probing and insertion of silicone tubes may be attempted, but neither technique is very successful. More recently, attempts to dilate the sac and duct have been undertaken with a balloon catheter passed through the normal system or via an opening made through the lacrimal fossa into the nose [83].

4.8 Chalazion

A chalazion is a focal inflammatory lesion of the eyelid that results from the obstruction of a sebaceous gland, either meibomian or Zeis. Extravasated lipid material produces a surrounding chronic lipogranulomatous inflammation. A chalazion may occur acutely with eyelid edema and erythema and evolve into a nodule, which may point anteriorly to the skin surface or, more commonly, through the posterior surface of the lid. The lesion may drain spontaneously or persist as a chronic nodule, usually a few millimeters from the eyelid margin. Lesions also may appear insidiously as firm, painless nodules (Fig. 4.24). Large lesions on the upper lid may even induce astigmatism. Chalazia often occur in patients with blepharitis and rosacea. These lesions may be mistaken for other more serious lesions such as malignancies [84].

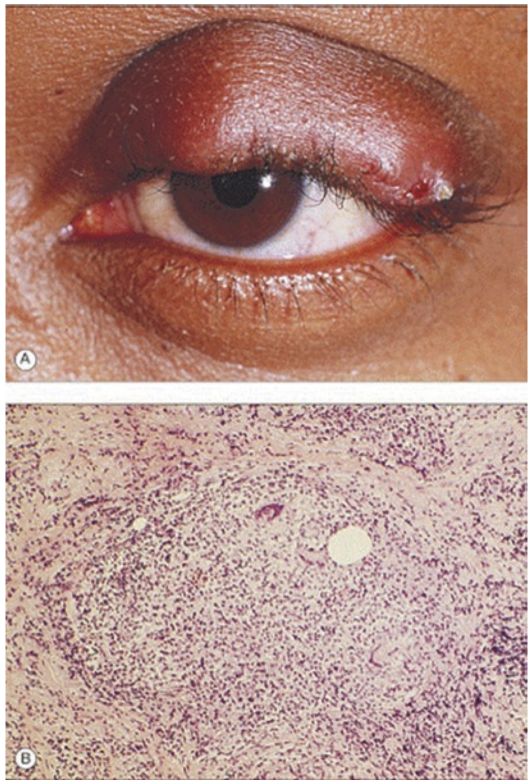

Fig. 4.24 Chalazion and external hordeolum. (**a**) The medial lesion of the upper eyelid appeared as a firm, painless nodule, consistent with a chalazion. The lateral lesion caused pain and eyelid erythema, subsequently becoming more localized, with drainage of purulent material through the skin surface. (**b**) A clear, circular area surrounded by epithelioid cells and multinucleated giant cells can be seen. In processing the tissue, lipid is dissolved out, leaving a clear space

Diagnosis is based on the typical clinical features. Acute lesions appear similar to hordeola in appearance – differentiation is nearly impossible to make clinically. In recurrent or atypical lesions, a sebaceous gland carcinoma needs to be excluded; thus, histopathological examination is important. Histopathology reveals lipogranulomatous inflammation, with clear spaces corresponding to lipid, surrounded by foreign body giant cells, epithelioid cells, neutrophils, lymphocytes, plasma cells, and eosinophils. A fibrous pseudocapsule may form around a lesion.

Treatment varies according to the stage of a lesion. Acute lesions are treated with hot compress to encourage localization and drainage. Chronic chalazia may be treated using intralesional corticosteroid injection or surgical drainage. Vertical transconjunctival incisions allow adequate exposure of lesions and limit damage to surrounding meibomian glands. Small chalazia, which may resolve spontaneously, can be removed with incision and curettage.

4.8.1 Hordeolum

A hordeolum is an acute purulent inflammation of the eyelid. An external hordeolum, or stye, results from infection of the follicle of a cilium and the adjacent glands of Zeis or Moll. The lesion typically causes pain, edema, and erythema of the eyelid, which becomes localized and often drains anteriorly through the skin near the lash line (see Fig. 4.24). An internal hordeolum occurs due to obstruction and infection of a meibomian gland. Initially, a painful edema and erythema localizes as an inflammatory abscess on the posterior conjunctival surface of the tarsus. In both external and internal lesions, cellulitis of the surrounding soft tissue may develop. Diagnosis is based on the clinical appearance and culture, with *Staphylococcus aureus* most frequently isolated. Hordeola frequently occur in association with blepharitis. Histopathology reveals an abscess or a focal collection of polymorphonuclear leukocytes and necrotic tissue.

Although the inflammatory process usually is self-limited, with drainage and resolution occurring within 5–7 days, hot compress and topical antibiotics help confine the spread of the lesion. Rarely, incision and drainage are necessary. Systemic antibiotics are used only if significant cellulitis exists. Treatment of accompanying blepharitis is helpful to prevent the formation of new lesions.

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Acute Disturbance/Loss of Vision

5

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Abstract

Acute visual loss is an important ophthalmologic emergency that may affect patients at all ages. Diagnosis and management of acute visual loss begin with taking a careful medical history and examination. Loss of vision may affect one eye or both eyes. It can be transient or permanent. Also, visual loss can vary from blurring to complete blackness. Monocular, transient visual loss which lasts <24 h, also referred to as amaurosis fugax, is usually caused by ischemic ophthalmologic diseases such as retinal emboli, carotid artery disease, giant cell arteritis, and retinal vein occlusion. Retinal migraine, optic neuropathy, papilledema, intermittent angle closure glaucoma, spontaneous hyphema, and orbital masses can also cause monocular visual loss. Temporary visual loss can be binocular, and it is generally caused by cerebral diseases such as migraine, head trauma, seizures, and vertebrobasilar ischemia. Permanent visual loss persists >24 h and usually affects one eye. The disease which causes persistent visual loss in one eye may affect the other eye in case of specific risk factors. Retinal vascular obstructions, optic neuropathies, vitreous hemorrhage, rhegmatogenous retinal detachment, stroke, and psychogenic visual loss are the most common causes of persistent visual loss. Management of acute visual loss varies according to the diagnosis. Visual outcome and prognosis may vary depending on the cause of visual loss, patient's risk factors, admission time to hospital, referral time, duration of diagnosis, and time to start treatment.

Keywords

Acute visual loss · Amaurosis fugax · Transient visual loss · Retinal emboli · Carotid artery disease · Retinal migraine · Persistent visual loss · Retinal artery occlusion · Retinal vein occlusion · Optic neuritis · Giant cell arteritis · Anterior optic ischemic neuropathy · Vitreous hemorrhage · Rhegmatogenous retinal detachment · Stroke

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Acute visual loss is a common, frightening complaint for patients with variable presentations. Acute vision loss is a major challenge in the emergency room because of the wide range of causes, the need for rapid evaluation, and treatment planning.

When a patient with acute visual loss is evaluated, the most important points are to determine the eye with visual loss, the degree and the duration of visual loss, and whether it resolves or not at the time of referral. In general, monocular vision loss usually indicates an ocular problem, and binocular vision loss is usually cerebral in origin. The loss of vision can be transient (lasts <24 h) or persistent (lasts >24 h).

Ocular pathologies in the differential diagnosis of sudden vision loss are vast. A careful history is key to eliminate most diseases in the differential diagnosis and will allow for a more focused physical examination. Prompt diagnosis and treatment may influence the visual outcome and prognosis.

This topic aims to present an overview of the approach to patients with acute visual loss.

5.1 Temporary Visual Loss

Amaurosis fugax (means "fleeting blindness") is a transient vision loss in one or both of the eyes. Some authors recommend that "amaurosis fugax" means lack of blood perfusion to the optic nerve and retina [1]. Since no etiological definition is available, acute and temporary vision loss in one or both of the eyes is preferred to define "transient monocular visual loss" (TMVL) and "transient binocular visual loss" (TBVL).

Temporary visual loss (TVL) is caused by several groups of disorders in a range of relatively benign and serious neurologic or ophthalmologic diseases. Obtaining a careful history, examining for localizing the problem to a visual pathway region, performing focused laboratory, and imaging tests and a differential diagnosis constitute the most important step for clinical evaluation of a patient with TVL presentation.

Since TVL patients mostly present after the resolution of visual disturbance, neurological and ophthalmological examinations revealed no abnormalities in many of the cases. Thus, the clinician may acquire valuable clues from the patient's history. Identification of the visual loss affecting one or both eyes, its duration, and specific visual symptom description is important.

TMVL generally implies a prechiasmatic disorder, such as ipsilateral carotid artery disease-caused ischemia. Therefore, the differentiation of homonymous visual field defects and monocular vision loss is important. It is essential to ask whether a visual loss was noticed also in the non-affected eye after covering the affected eye during attack since this defect is frequently mixed with monocular visual loss on temporal field defect side [2]. TBVL may be caused by chiasmatic lesion, retro-chiasmatic (optic tracts, or radiations, or the visual cortex) lesion, or bilateral prechiasmal lesions [3].

Duration of the vision loss is important to distinguish some benign or serious pathologies. Visual disturbances due to papilledema typically last for seconds [4], thromboembolic events generally last 1 to 15 min, and migraine aura often lasts 15 to 30 min [5].

TVL from any cause can be defined by many different expressions. Vision loss could vary from slight blurring to complete blackness and may involve partial or complete visual field. Ocular surface disorders or a similar relatively benign ophthalmic problem may cause mild vision blurring [6]. Half or whole of the vision field or small central or paracentral areas of it may be lost in ocular ischemia patients [7].

A precipitating factor may be helpful in TVL differential diagnosis. Postural changes may accompany papilledema, hypertension, carotid stenosis, and giant cell arteritis-caused TVL episodes [8–10]. While gaze-evoked TVL may be seen in orbital mass lesions or foreign bodies, demyelinating disorders are where heat-evoked TVL (Uhthoff's phenomenon) may be seen [11–13].

Age of the patient can give clinician useful clues. Benign reasons of TVL such as migraine is frequently common at younger patients; on the contrary, older patients often tend to have a more serious causes [3, 14]. Elderly patients tend to

have more associated diseases like diabetes mellitus, hyperlipidemia, and hypertension that all suggest atherosclerotic vascular disease.

The clinician needs to ask associated symptoms for differential diagnosis. Thromboembolic events are mostly painless. Headache or periocular pain should suggest migraine, giant cell arteritis, or angle-closure glaucoma. Symptoms like vertigo, diplopia, and dysarthria can be seen at vertebrobasilar artery insufficiency [15]. Transient contralateral hemiplegia with TVL should suggest severe carotid stenosis [16].

5.1.1 Etiology of Transient Monocular Visual Loss

5.1.1.1 Retinal Emboli

Retinal emboli are the most common cause of TMVL [17] Most commonly, emboli originate from an internal carotid artery-based atheromatous plaque [18]. Other emboli sources are the heart and the great vessels and paradoxical embolism [2, 19]. TMVL can rarely be caused by atrial myxoma, air, septic, fat, silicon, or talc emboli [20–26]. Complete blackness is the phrase usually used to describe visual loss. The duration of TMVL is typically less than 15 min. Underlying cause can be reached through treating TMVL from retinal embolism.

5.1.1.2 Carotid Artery Disease

Severe ipsilateral internal or common carotid artery stenosis or occlusion (90–100%) that caused hypoperfusion may cause TMVL [27]. While exposure to bright light is often the inducing factor, activities such as meals (postprandial vascular steal), postural changes, or sexual activity and similar activities reducing ocular perfusion pressure are also the causes [28–32]. Ocular ischemic syndrome signs which can be seen are ocular hypotension or hypertension, iris or angle neovascularization, disc or retinal neovascularization, retinal hemorrhages, and aqueous flare [33]. The common description of visual loss is a curtain or shade covering the vision which can last from seconds to minutes (Fig. 5.1). Contralateral hemispheric symptoms due to hypoperfusion can be seen with vision loss [31]. Stroke risk increasing approximately 2–3% per year is why carotid stenosis or occlusion diagnosis and treatment are important [34]. Carotid endarterectomy, carotid artery stenting, and medical management are the treatment options for symptomatic carotid atherosclerotic disease [35, 36]

Fig. 5.1 An angiography of a patient who has experienced a few times of temporary visual loss shows about 95% stenosis in the proximal left internal carotid artery

5.1.1.3 Giant Cell Arteritis

GCA presents with TMVL in 10–30% of patients TMVL which has been related with poor visual prognosis [37]. TMVL prior to permanent visual loss has been reported to affect approximately 50–65% of patients [38]

5.1.1.4 Retinal Vein Occlusion

Although permanent visual loss is usually caused by retinal vein occlusion, the premonitory symptom may be TMVL [39]. Typical description of visual loss is “cloudy vision,” and it may last several hours.

5.1.1.5 Retinal Migraine

Anterior visual pathway migraine, eye migraine, and visual migraine are some examples for the terms used for retinal migraine which should not be confused with classic migraine aura [40]. Idiopathic and reversible monocular vision loss

is the definition made by the International Headache Society for retinal migraine which is followed by a typical migraine headache within 60 min, and it is considered a diagnosis of exclusion [41]. It is thought that retinal vasospasm is the cause of visual loss [42]. During an attack of retinal migraine, afferent pupil defect can be detected [3]. Calcium channel blockers are effective for treating some patients [43].

5.1.1.6 Optic Neuropathy (Uhthoff's Phenomenon)

Due to the increasing body temperature (e.g., hot shower, exercise), TVL episodes may occur in chronic and demyelinating optic neuropathy patients [44, 45]. Visual loss lasting minutes to hours returns to the baseline visual acuity with the body temperature returning to the normal ranges. A demyelinated optic nerve with a temporary conduction block is considered as the cause. No specific treatment is required.

5.1.1.7 Papilledema

Papilledema is an important cause of TVL (Fig. 5.2). A partial or complete "whiting" or "graying out" in the visual field called as transient visual obscuration episodes lasts for seconds [46]. Episodes may be spontaneous or may occur together with intracranial pressure increasing postural changes and maneuvers like coughing and straining.

5.1.1.8 Intermittent Angle-Closure Glaucoma

Intermittent angle-closure glaucoma is characterized with TMVL, halos around lights, and eye pain due to increased intraocular pressure [47, 48]. Diagnosis can be made by gonioscopy. Laser iridotomy is applied in the treatment.

5.1.1.9 Spontaneous Hyphema

Spontaneous hyphema can occur in patients who had cataract surgery with intraocular lens implantation (uveitis-glaucoma-hyphema syndrome) [49]. The patient usually describes a rapid reduction in vision over minutes or red vision (erythropsia), lasts hours to days.

5.1.1.10 Orbital Masses and Foreign Bodies

TVL occurs with a certain eccentric gaze position and usually arises from intraorbital masses and foreign bodies [50]. It is also called gaze-evoked amaurosis, and vision loss recovers when the eye moves back from eccentric gaze.

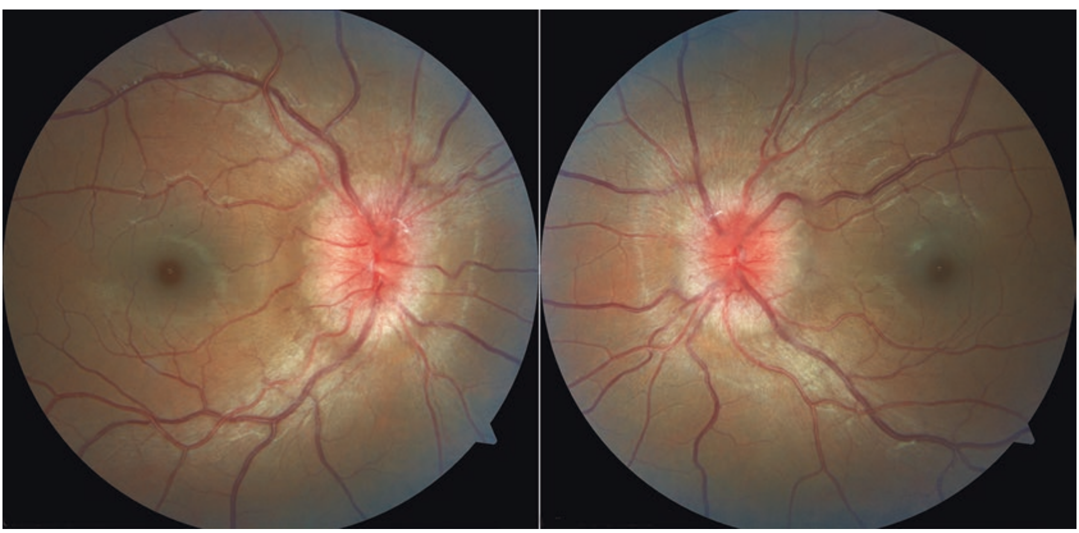

Fig. 5.2 Patient with bilateral papilledema due to idiopathic intracranial hypertension. Patient suffers from headache and transient flashes and visual loss after waking up

5.1.2 Etiology of Transient Binocular Visual Loss

5.1.2.1 Migraine

Episodic, binocular, and transient visual loss is caused mostly by migraine aura in young adults [51]. 15 min or longer is the usual duration of classic visual aura and rarely lasts more than 60 min. The duration of a classic visual aura is usually 15 min or longer, lasting more than 60 min rarely. An angulated scintillating edged achromatic or black and white figure or a similar positive visual phenomenon before scotoma or vision loss constitutes its usual start. A unilateral headache associated with a photophobia, nausea, phonophobia, and vomiting typically follows. Visual aura without headache may occur in some patients. These patients are usually elder and have had previous migraine attacks with visual aura. In basilar-type migraine, a transient cortical blindness or homonymous visual field loss producing aura without an associated positive visual phenomena may occur [52]. Diplopia, vertigo, ataxia, and a decreased consciousness level may associate with this type of migraine [53].

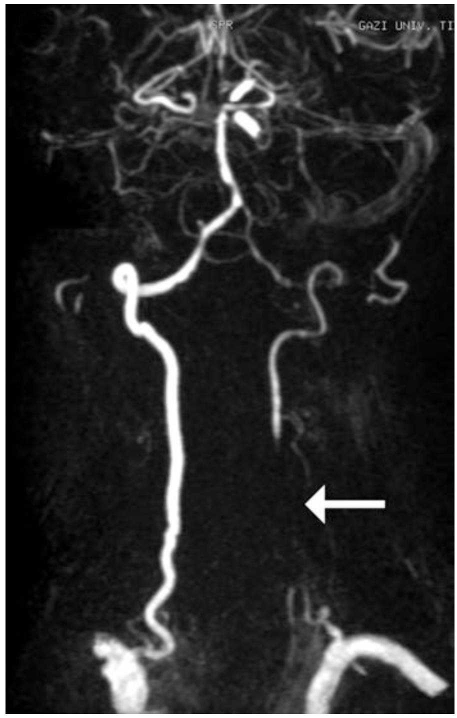

Fig. 5.3 Patient with vertebrobasilar insufficiency. Supra-aortic MR angiography showed no flow from the ostium in the left vertebral artery and retrograde filling from the right vertebral artery at the distal side

5.1.2.2 Head Trauma

A blunt and occipital head trauma may rarely cause transient and cortical vision in children or adolescents [54, 55]. It develops within minutes after trauma and lasts minutes to hours. Clinician should exclude a possible intracranial hemorrhage with neuroimaging [55].

5.1.2.3 Occipital Seizures

Occipital seizures typically cause a sudden start of binocular positive visual phenomena with visual loss in a specific part of the visual field [56]. Over the course of the seizure, positive visual phenomena symptoms may increase in size, move, and multiply. They usually last a minute. Prolonged ictal blindness may occur rarely, and it is called as status epilepticus amauroticus [57]. Postictal visual loss lasts minutes to hours, and postictal headache may be seen together.

5.1.2.4 Vertebrobasilar Ischemia

Posterior cerebral artery occlusion may cause occipital lobe ischemia which usually causes isolated TBVL [58]. Vertebrobasilar ischemia may result in TBVL with dysarthria, vertigo, diplopia, and dysphagia and such associated brainstem ischemia symptoms or hemisensory loss, hemiparesis, and aphasia and such cerebral ischemia symptoms (Fig. 5.3). Ischemia may arise from thrombosis, embolism, or hypoperfusion [59].

5.2 Persistent Visual Impairment

5.2.1 Retinal Artery Occlusion

Retinal artery occlusions are divided anatomically into central and branch artery obstructions. The most of retinal artery occlusions originate

from either thrombotic or embolic events [60]. Central and branch retinal artery occlusion demonstrates no difference in emboli source and type. But compared to central retinal artery occlusion, branch retinal artery occlusion tends to be more embolic [61]. Inner retinal layers are affected at retinal artery occlusions because outer layers are supplied by choroidal circulation. Retinal artery occlusion occurs rarely, and visual loss is usually severe and permanent. All retinal artery occlusion-diagnosed patients should take a systemic evaluation, because there is a strong association with systemic diseases.

5.2.1.1 Central Retinal Artery Occlusion

The estimated annual incidence rate is 1.3 in 100,000 in the occlusion first described by Von Graefe in 1859, and men are affected more than women [62–64]. Bilateral involvement occurs rarely (1–2% of cases). The mean age is about 60 years.

Most central retinal artery occlusions (CRAO) are considered to be caused by thrombus formation at lamina cribrosa or just its proximal [65]. In some cases, central retinal artery (11.1%) or one of its branches (41.4%) may house emboli [66]. Central retinal artery occlusions may be caused by vasculitis, optic neuritis, direct optic nerve or blood vessel damage causing trauma, radiation retinopathy, emboli associated with depot medication injection around the eye, optic disc drusen, and prepapillary arterial loops [67–73].

About 40% of patients with CRAO have systemic arterial hypertension, and 20% have diabetes [74]. No specific cause for the CRAO can be found in over 50% of affected patients, but at least one undiagnosed vascular risk factor such as hyperlipidemia (36%), diabetes (12%), and hypertension (27%) was present in 64% of CRAO-diagnosed patients [74]. Embolic sources can be found in patients with a ratio less than 40%. Nearly 30% of the affected patients had hemodynamically significant ipsilateral carotid artery occlusion [17]. Coagulopathies such as antiphospholipid antibodies, protein C-S deficiency, and antithrombin III deficiency are other associated systemic diseases [75].

Sudden, painless visual loss is the most characterized symptom of the central arterial occlusion. Visual acuity generally decreases (<20/800), but vision can be maintained if the cilioretinal artery is present. Afferent pupillary defect is always present on the affected side [76].

Fundus may appear normal in first few minutes to hours after the occlusion. Decreased blood flow that caused obstructed artery area ischemic retinal whitening is the most important finding on fundus examination [65]. A cherry-red macular spot is typical. As a result of thin nerve layer in the macula, normal choroidal blood flow causes this finding. The arteries may be seen thin and attenuated. Splinter retinal hemorrhages are common on the disc, but alternative diagnosis should be suggested when extensive. A normal-looking small retinal area is caused by a patent cilioretinal artery.

Fluorescein angiography typically shows delayed arm-to-retina time or absent retinal arteriolar blood flow [77]. Inner retinal thickening with shadowing of the outer retina can be seen at optical coherence tomography (OCT) in the acute phase [78]. In the electroretinography, a decreased to absent b-wave with intact a-wave is shown [79]. Remaining peripheral vision temporal island can be seen in visual field examination.

Systemic evaluation must include fasting cholesterol, fasting glucose, C-reactive protein, blood pressure, erythrocyte sedimentation rate, platelet count, duplex carotid ultrasound, and echocardiogram. In young patients (<50 years), hypercoagulable screening, vasculitic markers, and chest film must be taken.

In the management of CRAO, acute interventions aim to restore central retinal artery perfusion. Late admission to hospital and rare occurrence of the disease are the major barriers to acute treatment for CRAO. No proven treatment or guideline-based therapy is available. Inhalation of carbogen (95% oxygen, 5% carbon dioxide) doesn't seem to be effective [80]. Hyperbaric oxygen can be used for increasing retinal oxygenation with promising results [81, 82]. Retinal arterial blood flow can be increased by ocular

massage to dislodge emboli, anterior chamber paracentesis, ocular antihypertensive medications such as intravenous mannitol and acetazolamide, and vasodilating agents (sublingual isosorbide dinitrate or systemic pentoxifylline) [83]. Reversal of arterial occlusion is attempted by the use of embolus dissolution with laser [84]. Intravenous fibrinolysis efficacy has been shown in studies with experiencing an improvement in vision acuity up to 6 h of onset [85, 86].

The retinal whitening usually resolves in 6 weeks, and optic disc pallor and arterial collaterals may develop [17]. Iris neovascularization occurs in about 18%, and then optic disc neovascularization occurs in nearly 2% of patients [87]. Panretinal photocoagulation reduces the risk of neovascular glaucoma moderately.

The long-term CRAO management should identify systemic risk factors and reduce secondary ischemic events (cerebral stroke and acute coronary syndrome).

5.2.1.2 Branch Retinal Artery Occlusion

Branch retinal artery occlusion (BRAO) is a rare retinal vascular disorder, even more than CRAO [88]. The most of BRAOs are caused by retinal artery emboli [89, 90]. The emboli can be seen at fundus examinations. There are three types of emboli: cholesterol, calcific, and platelet-fibrin. Ipsilateral carotid artery atheromatous plaques are the typical origin of cholesterol emboli. Platelet-fibrin emboli generally arise from carotid or cardiac thrombosis. Calcific emboli usually associated with calcific heart valves or aorta.

In general, sudden, painless loss of vision or scotoma occurs in BRAO. The most important finding on fundus examination is retinal whitening that corresponds to the areas of the ischemic retina (Fig. 5.4). Retinal emboli can be seen in over two-thirds of BRAO [90, 91]. Ancillary testing, differential diagnosis, and systemic associations are similar to CRAO.

No efficient treatment is proved for BRAO.

As the branch retinal artery obstruction visual prognosis is much better than central retinal artery obstruction, invasive therapeutic interventions are not performed because of the complications of the therapy. Ocular massage or paracentesis may dislodge emboli, and laser treatment has been shown successful in some cases [84, 92, 93].

Fig. 5.4 Retinal arteriolar branch occlusion caused by multiple retinal emboli due to internal carotid artery atheromatous plaque

Most patients' visual prognosis is better than CRAO, and a fixed visual field defect and good visual acuity remain. Retinal neovascularization is uncommon, and iris neovascularization does not occur generally.

5.2.1.3 Cilioretinal Artery Occlusion

Nearly 30% of the population has cilioretinal artery [94]. Cilioretinal artery perfuses papillomacular bundle area (Fig. 5.5). As it is directly posterior ciliary circulation derived, it may remain patent in CRA [89]. The prognosis is relatively good [95]. A bad visual prognosis is available in cilioretinal artery occlusion with ischemic optic neuropathy, and it is usually temporal arteritis related [96, 97].

5.2.2 Retinal Vein Occlusion

The second most common retinal vascular disorder is retinal vein occlusion (RVO). RVOs have an estimated prevalence of 0.5% and incidence of 2.3% according to the latest studies [98, 99]. Persistent visual loss may occur in patients who

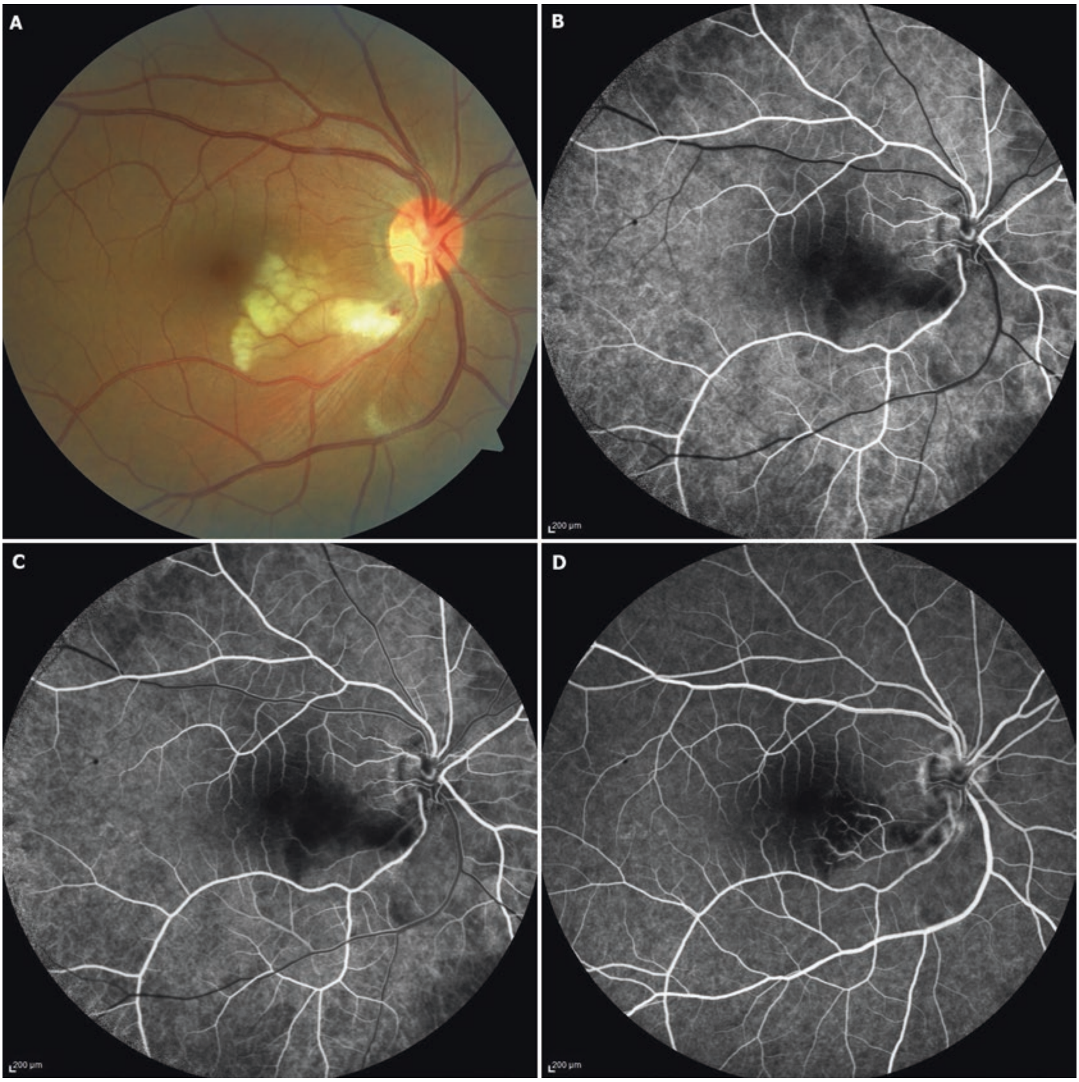

Fig. 5.5 Patient with cilioretinal artery occlusion. (**a**) Ischemic whitening of the cilioretinal area. (**b**, **c**, and **d**) Delayed cilioretinal arteriolar blood flow was seen in the fundus fluorescein angiography

suffer RVO. The most important visual loss cause is macular edema [100–102]. The other reasons are ischemia, retinal neovascularization, neovascular glaucoma, and vitreous hemorrhage [103, 104]. RVOs can be divided into central retinal vein or branch vein occlusion [105]. CRVO and BRVO prevalence is 0.08% and 0.4% [106].

Although there are many diseases such as hypertension, hyperlipidemia, and atherosclerotic cardiovascular disease associated with RVO, they are not directly related [107, 108]. Major risk factor for RVO is hypertension in elderly patients [107, 109]. However, coagulopathies are the most common cause of RVO in

younger patients [110–113]. Other conditions associated with RVO are collagen vascular diseases, use of oral contraceptive pills, and ocular conditions such as glaucoma, trauma, and retinal vasculitis [114, 115].

The findings of the fundus examination are engorgement and dilatation in retinal veins with intraretinal hemorrhages and edema, cotton-wool spots, retinal exudates, and macular edema in RVO [116]. Anterior segment examination with slit-lamp biomicroscopy should always be performed. Iris and angle neovascularization can be detected early by iris vascular congestions [63, 117].

Systemic evaluation should be performed in all patients. This must include blood pressure measurement, full blood count, fasting blood glucose, fasting cholesterol levels, serum creatinine, urea and electrolytes, thyroid function tests, and electrocardiogram. Workup for blood testing in young patients must include thrombophilia screening for hyperviscosity and hypercoagulable states, inflammation markers, rheumatological markers, and treponemal serology. Elevated hematocrit and fibrinogen levels are known to be a poor clinical outcome in RVO patients.

5.2.2.1 Central Retinal Vein Occlusion

Venous outflow obstruction at the same level or its posterior causes vein occlusion in the central of the retinal (CRVO) [118].

CRVO patients usually suffer sudden and painless visual loss (Fig. 5.6). Typical fundus examination of CRVO such as hemorrhages in all four quadrants, cotton-wool spots, optic disc, and macular edema can be confirmed by delayed arteriovenous transit time at fluorescein angiography [119]. Other findings can be optic nerve head leakage, perivenous staining, late leakage in the macular area, and petaloid pattern that indicates macular edema.

Ischemic and nonischemic are the types of CRVO, which often caused by clotting and thrombosis of retinal vein and induces an ischemic and hypoxic state [120]. The diagnosis of an ischemic or nonischemic CRVO is usually based on the examination, fluorescein angiography findings, and electroretinogram [121]. Nearly two-thirds of patients who have the ischemic CRVO may develop ocular neovascularization [122]. The patients with ischemic CRVO have usually poor visual prognosis.

The prognosis of CRVO in young patients was better than elder patients [99]. Coagulopathies causing CRVO are often reported to be nonischemic. CRVO can occur in young healthy patient with no known systemic or ocular problem with a relatively benign condition known as papillophlebitis [123]. It is an uncommon condition caused by secondary venous congestion due to central retinal vein inflammation at lamina cribrosa level.

Initial visual acuity is the most important visual acuity outcome factor [124]. Sixty-five percent of patients with a good initial visual acuity (20/40 or higher) were able to provide good visual acuity. Patients with low initial visual acuity (20/200) probably had a poor visual outcome.

Nonperfusion and ischemia most rapidly develop in the first 4 months [124]. Low initial visual acuity and the area size of nonperfused retina seen on fluorescein angiography are the most important factors for iris and angle neovascularization. Extensive retinal hemorrhage and venous tortuosity are other risk factors. In studies, there was a correlation between initial visual acuity, older age, male sex, systemic vascular risk factors, and glaucoma and poor visual outcome and development of retinal ischemia [125].

Optical coherence tomography is very useful to detect macular edema and serous macular detachment in patients with CRVO [126]. Visual loss is not always related to degree of the edema. But the changes of inner segment/outer segment junction line due to loss of photoreceptors are directly related to poor visual acuity [127]. Epiretinal membrane, vitreous macular adherence, lamellar macular hole, and intraretinal exudate are also common in optical coherence tomography testing in the setting of a CRVO.

Treatment that reverses the pathology seen in CRVO is unknown. It is important to reduce risk factors along with a healthy diet and exercise. But, complications such as macular edema and neovascularization should be treated because these complications are related with visual loss.

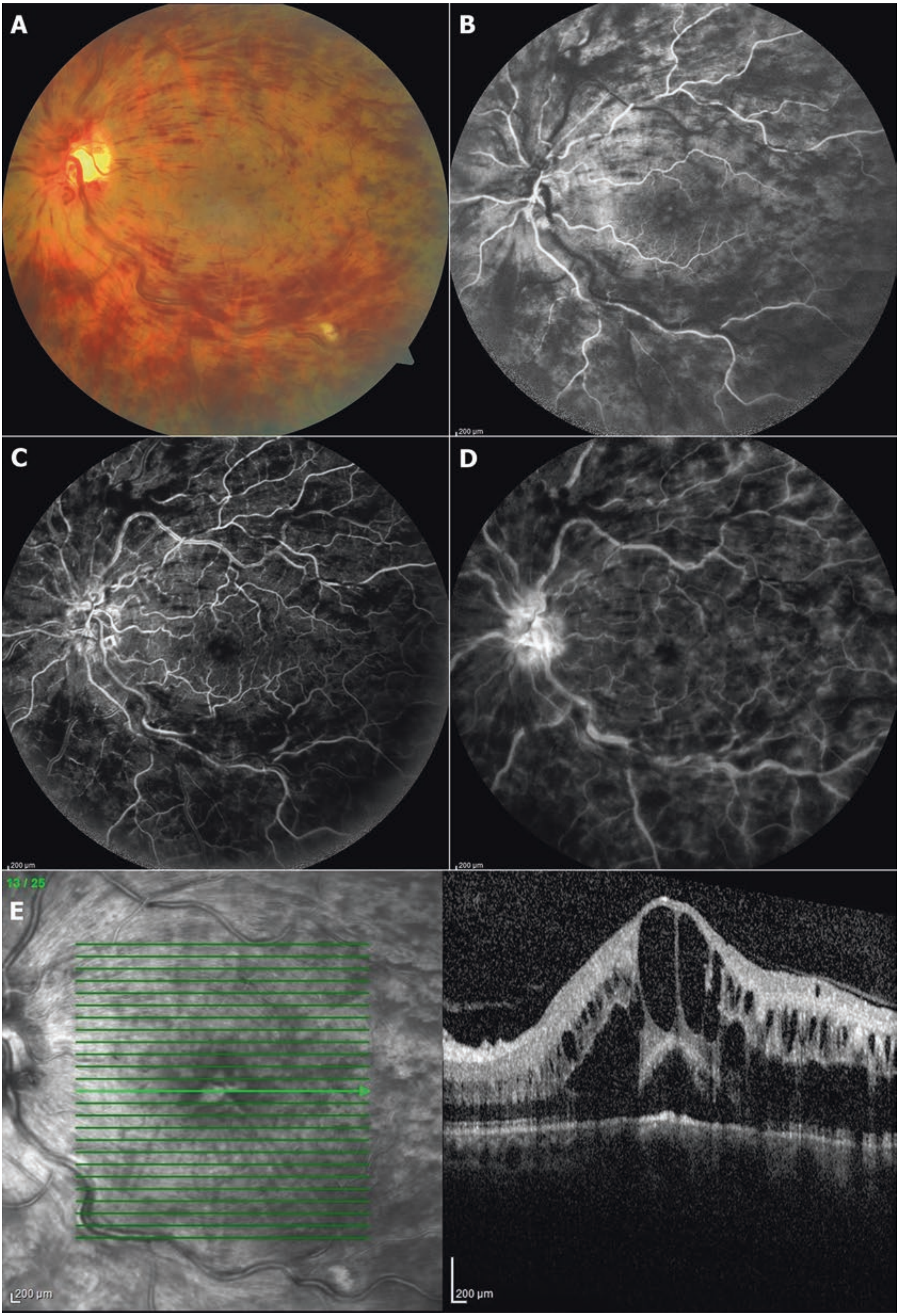

Fig. 5.6 Ischemic central retinal vein occlusion patient. (**a**) Hemorrhages in all four quadrants and cotton-wool spots in the fundus photography. (**b**) Hypofluorescence areas due to either blockage of intraretinal hemorrhages in early phase of fundus fluorescein angiography can be seen. (**c**) Delayed arteriovenous time. (**d**) Ischemic retina in fundus fluorescein angiography late phase. (**e**) Macular edema and serous macular detachment in the optical coherence tomography

The treatment of macular edema includes anti-VEGF pharmacological agents such as bevacizumab, ranibizumab, aflibercept, and intravitreal steroids (Fig. 5.7). Other rare treatment modalities are laser photocoagulation and surgical options such as pars plana vitrectomy, retinochoroidal anastomosis, and radial optic neurotomy.

Increased level of VEGF caused by retinal hypoxia is strongly correlated with macular edema and neovascularization [128]. CRUISE study was the first study to show that ranibizumab is effective in macular edema treatment in CRVO [129, 130]. This study compared the efficacy of ranibizumab 0.3 mg or 0.5 mg with sham injection. Patients received monthly injections for 6 months and shifted to a pro re nata (PRN) protocol. Both 6-month and 12-month results showed that ranibizumab was successful both anatomically and functionally compared to sham injections.

SHORE study which compared monthly injections for 12 months with CRUISE treatment protocol showed that there was no difference statistically [131]. Similar long-term outcomes of ranibizumab treatment were provided by HORIZON and RETAIN studies.

HORIZON was the extension study for CRUISE study [132]. PRN regimen was applied with 3-month follow-ups. Baseline-compared average visual acuity change at 24 months was +9.4, +14.9, and +16.2 letters in the sham/0.5 mg, 0.3/0.5 mg, and 0.5/0.5 mg groups. Visual acuity reduced 4.2, 5.2, and 4.1 letters in the sham/0.5 mg, 0.3/0.5 mg, and 0.5 mg groups, when compared with CRUISE study. Authors concluded that the reduced follow-up and lower number of injections in the second treatment year were associated with visual loss in CRVO patients in the second year.

Twenty-seven patients completed 2-year follow-up in the HORIZON study and, as a HORIZON extension trial, enrolled in the RETAIN study [133]. RETAIN showed that poor responders to the ranibizumab require more frequent injections and gain less letters. In contrast, early responders had superior long-term visual outcomes with either 0.3 mg or 0.5 mg.

COPERNICUS and GALILEO are phase III randomized, multicenter trials which evaluated the efficacy of aflibercept on macular edema due to CRVO. In COPERNICUS study, 56% of aflibercept-treated eyes and 12% of eyes in the sham group gained ≥15 letters at 6 months [134, 135]. PRN doses of aflibercept 2 mg every 4 weeks were applied after 6 months till 12 months. At 1 year, visual acuity gain was 16.2 letters in aflibercept + PRN group and 3.8 letters in sham + PRN group. The similar results were obtained by the GALILEO study showing 18 letters gain by 6 months, 16.9 letters at 1 year, and 13.7 letters at 76 weeks [136, 137].

Comparison of data between different trials is difficult due to different baseline including criteria and primary/secondary end points [138]. COPERNICUS trial had 15.5% of patients with ischemic CRVO and 8.2% of the patients in the GALILEO trial compared to 0.5% of the patients in the CRUISE study. Besides, CRUISE study excluded the patients with afferent pupillary defect but aflibercept studies did not. The duration of macular edema was longer in aflibercept studies.

Intravitreal bevacizumab has also been used to treat CRVO with macular edema. Epstein et al. compared that the treatment protocol of bevacizumab 1.25 mg every 6 weeks for 6-month duration achieved 14.1 letters gain at 24 weeks in bevacizumab group [139]. A decrease of 20 letters was obtained in sham group. Although bevacizumab is reported to have a similar effect as ranibizumab in macular edema treatment caused by CRVO in various studies, its use is mainly off-label.

The effectiveness of intravitreal steroids has been evaluated in SCORE and GENEVA trials [140, 141]. Two different dosed dexamethasone implants (0.7 and 0.35 mg) were used in GENEVA study. At 2 months, 29% of CRVO patients in the 0.7 mg and 33% of CRVO patients in the 0.35 mg groups gained ≥15 letters improvement compared with 9% CRVO patients in the sham group [141]. However, the results at 6 months were not significant as the percentages dropped to 18%, 17%, and 12% for the 0.7 mg, 0.35 mg, and the sham group.

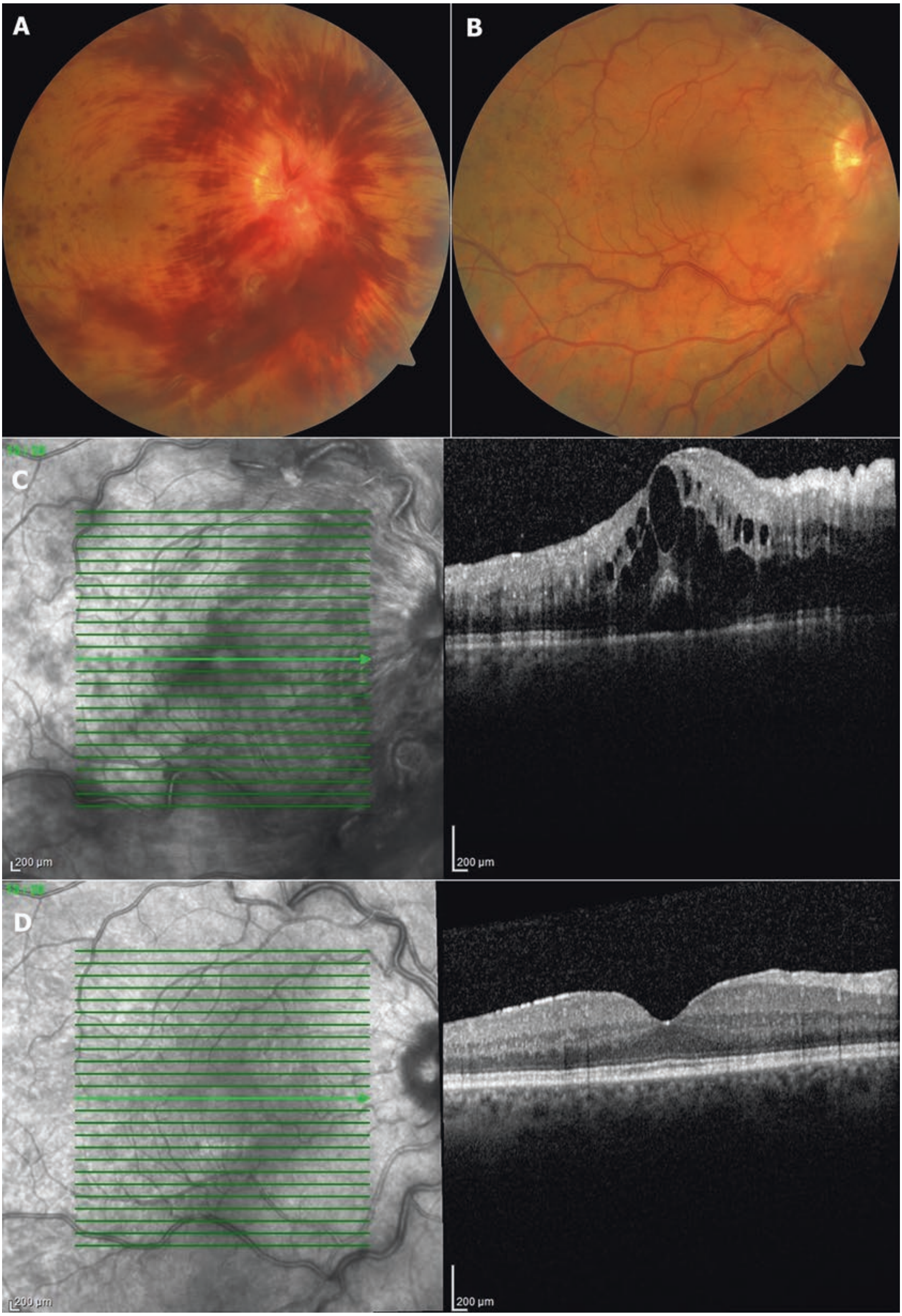

Fig. 5.7 A central retinal vein occlusion patient was referred by our clinic. (**a**) Fundus photography demonstrates preretinal hemorrhages in all retinal quadrants. (**b**) 3 months after A. Hemorrhages was cleared spontaneously. (**c**) Macular edema and serous macular detachment was detected in the optical coherence tomography at referral.

Ischemic CRVO patients are at high secondary neovascular glaucoma risk especially within the first few months of diagnosis. Reducing VEGF load by peripheral ischemic retinal ablation is the aim of scatter PRP laser. The RELATE study showed that scatter PRP laser has no benefit on visual acuity, edema resolution, and anti-VEGF injection number [142]. Scatter PRP laser is only recommended to reduce the risk of neovascularization of the anterior segment, retina, or optic disc [143].

Pars plana vitrectomy for the persistent macular edema due to CRVO can be beneficial, but clinician should remember that vitrectomy surgery may reduce the duration of the intravitreal anti-VEGF agents in the vitreous cavity when needed [144, 145]. Radial optic neurotomy is an alternative surgical treatment for CRVO. It is thought that neurotomy relieves central retinal vein pressure at lamina cribrosa site [146–148]. Limited results from retrospective studies were obtained, and severe complications such as hemorrhages, visual field defects, and retinal detachment were reported. Surgical treatment is not preferable anymore.

5.2.2.2 Branch Retinal Vein Occlusion

Branch retinal vein occlusion is more common than CRVO (106). Branch retinal vein occlusion (BRVO) causes acute visual loss which is usually caused by macular edema, vitreous hemorrhage, or macular ischemia [149–151]. Characteristic fundus finding is flame-shaped intraretinal hemorrhages which corresponded to the distribution of a retinal vein with a triangular configuration [152]. Twenty percent of BRVO cases develop retinal neovascularization within first 6–12 months, but anterior segment neovascularization and neovascular glaucoma are rare, in contrast to CRVO.

The diagnosis of an acute BRVO is usually made on fundus examination findings (Fig. 5.8). Fundus fluorescein angiography and optical coherence tomography are useful tools for detecting ischemia and macular edema, similar to CRVO [153–155].

In order to show the effect of intravitreal steroids and intravitreal anti-VEGF agents in the treatment of BRVO-caused macular edema, many prospective randomized clinical trials were made [156–162]. Effect of ranibizumab on BRVO was evaluated by BRAVO study [163]. At 6 months, the study showed a gain of ≥15 letters in more than 50% of the patients treated with ranibizumab monthly. Sixty-seven percent of BRVO patients completing the 12-month BRAVO trial [132] were included in HORIZON study. Patients maintained their visual acuity for the first 12 months of the HORIZON trial for BRVO patients. The reduction in frequency of ranibizumab injections with the PRN regimen during this second year of HORIZON study had minimal functional or anatomical effect in BRVO patients, in contrast to CRVO patients whom visual gain reduced. This difference can be attributed to lower retinal ischemia and VEGF peak seen in BRVO compared to CRVO. The SCORE study which compares intravitreal triamsinolon injection with control group for macular edema caused by BRVO showed no benefit in visual acuity [164]. GENEVA trial included BRVO patients also and showed that dexamethasone intravitreal implants (both 0.7 mg and 0.35 mg) are effective in the treatment [141].

In BRVO, scatter PRP laser is usually performed to the portion of the retina in the distribution of the occluded vein when there is a severe neovascularization [142, 165].

Arteriovenous sheathotomy aims to decompress the thickened and rigid arteriosclerotic artery at the arteriovenous crossing for improving retinal blood flow in BRVO [105]. This procedure includes pars plana vitrectomy, internal limiting membrane removal, and incision of sheath

Fig. 5.7 (continued) Ranibizumab treatment was planned and monthly injections started. (**d**) Optical coherence tomography image after six doses of ranibizumab injection. Macular edema and serous detachment was resolved with increasing of visual acuity

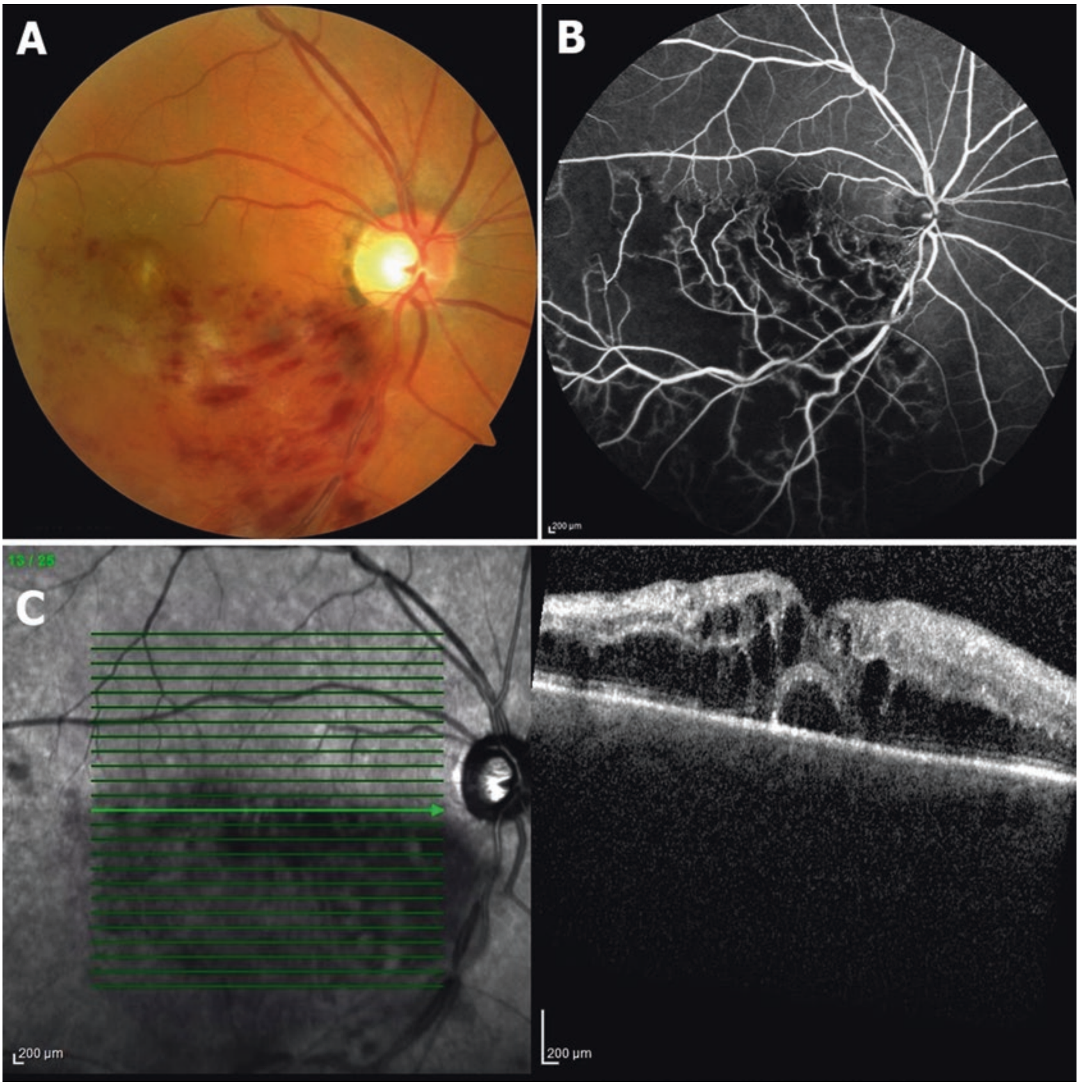

Fig. 5.8 Branch retinal vein occlusion patient. (**a**) Inferotemporal branch vein occlusion caused retinal hemorrhages and soft exudates. (**b**) Ischemia at the inferotemporal quadrant was seen in the fundus fluorescein angiography. (**c**) Cystoid macular edema with subretinal fluid caused by branch retinal vein occlusion was seen in optical coherence tomography

at the arteriovenous crossing site [105, 166]. The results for visual outcome are conflicted, and it is thought that it gives similar results with intravitreal agents.

5.2.3 Optic Neuropathy

Optic nerve damage due to any cause is named as optic neuropathy. The main symptom is vision loss with color vision deficiency. Most common optic neuropathy causes are optic neuritis and ischemic optic neuropathy [167]. Other causes are trauma and toxic, infiltrative, and genetic diseases affecting the optic nerves.

5.2.3.1 Optic Neuritis

Optic neuritis (ON) is optic nerve inflammation and constitutes an interdisciplinary challenge. Estimated incidence of ON is 1–5 per 100,000

persons [168]. Seen more commonly in women, most of the patients are between 15 and 45 years old [169]. Multiple sclerosis (MS) occurs in about 25% patients with optic neuritis, which is also known as demyelinating optic neuritis [170]. MRI studies showed that 34–74% of patients with optic neuritis was diagnosed with MS at the long-term follow-up [171, 172]. Demyelinating optic neuritis may present as isolated optic neuritis, neuromyelitis optica, and neuroretinitis. Other etiologies causing optic neuritis are vasculitis, postinfectious, and inflammatory [173].

The disease typically begins with eye pain with movement, followed by a subacute, unilateral visual loss 1–5 days later with loss of color vision and contrast sensitivity (Fig. 5.9). In some cases, especially in children, ON could be bilateral [174]. Visual field loss is common due to optic nerve inflammation, and it could be diffuse or focal. Defects in central visual are more common than peripheral visual field loss [175]. Afferent pupillary defect is a typical finding in ON patients if the disease is unilateral.

ON could be divided into retrobulbar neuritis and papillitis. In retrobulbar neuritis which is seen in two-thirds of the patients, the optic disc has a normal appearance [176]. ON is presented as papillitis in one-third of the patients, and swelling is present on the optic disc in fundus examination. Disc hyperemia, nerve fiber layer edema, and blurring of disc margins accompany optic disc edema.

Atypical form of optic neuritis, neuromyelitis optica (NMO), affects both the optic nerve and spinal cord. Known as Devic's disease, transverse myelitis-accompanying optic neuritis characterizes it [177]. The discovery of an antibody against aquaporin-4 (anti-AQP4) which was specific for NMO helped to differentiate NMO from MS [178]. The incidence of NMO is ranging from 0.053 to 0.4 per 100,000 persons [179, 180]. The disease causes acute visual loss with loss of sphincter control and paraparesis or tetraparesis [181]. In 2006, diagnostic criteria for NMO were published: ON, acute myelitis, and, at least two of three supportive criteria which are contiguous spinal cord MRI lesion extending over ≥3 vertebral segments, cranial MRI not meeting diagnostic criteria for MS, and positive anti-AQP4 [182] constitute diagnostic criteria.

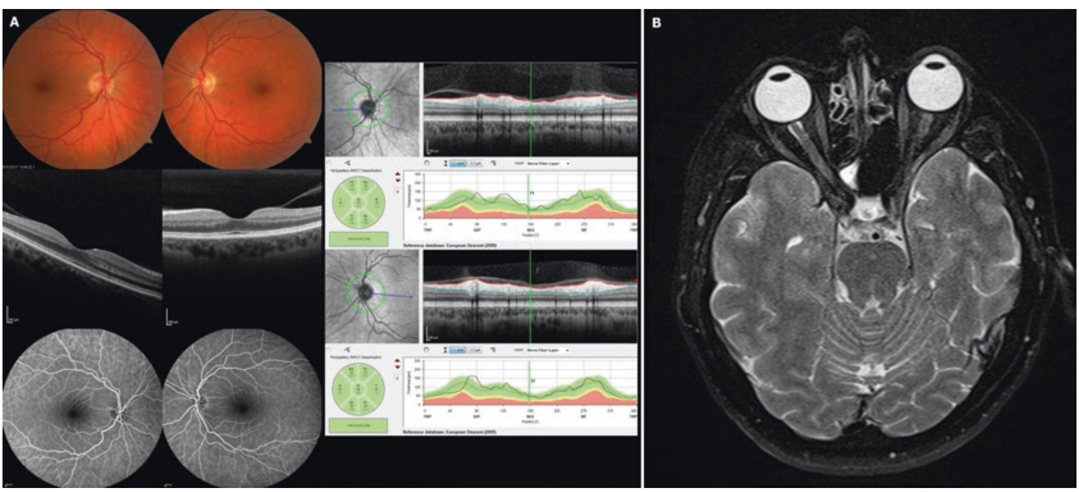

Fig. 5.9 A 51-year-old patient without any significant past medical history presenting with painless, sudden visual loss in the right eye. Best corrected visual acuity was 0.05 for the right eye and 1.0 for the left eye. There was no pathology in optical coherence tomography, fundus examination, retinal nerve layer thickness, and fundus fluorescein angiography (**a**). Axial, fat-suppressed, post-contrast, T2-weighted image demonstrates partial thickness and contrast enhancement of the nerve sheath. Retrobulbar neuritis was diagnosed, and the patient was treated for 3 days with methylprednisolone 1 g/day intravenously and oral prednisone treatment with a dose of 1 mg/kg/day following it. One week after steroid administration, visual acuity was increased to 0.7 in the right eye

Macular star and optic disc edema characterize neuroretinitis [183]. It is thought that inflammation of the optic neuritis spreads to the macula [184]. The disc is significantly swollen, and a stellate-shaped of hard exudates is seen in the macula [185]. The disease can be associated with some bacterial disease which may trigger immune response, such as *Bartonella*, *Borrelia*, syphilis, or idiopathic [186]. The treatment includes antibiotics steroids with 1 mg/kg/day dose, depending on the diagnosis and clinical progression.

Although signs and symptoms constitute the basis of ON diagnosis, laboratory and imaging tests are usually performed for evaluating the pathology. Laboratory test should be performed for the differential diagnosis of infectious and inflammatory etiologies including full blood count, C-reactive peptide, erythrocyte sedimentation rate, vitamin B12, syphilis markers, Lyme titer, ANA, ACE, and anti-ds DNA antibodies [184]. Cerebrospinal fluid analysis is important for MS. In patients with ON, cerebral and orbital magnetic resonance imaging (MRI) with fat suppression and gadolinium should be performed to evaluate demyelinating process and confirm the disease [187].

Optic Neuritis Treatment Trial (ONTT) is a level 1 study on treatment for optic neuritis [169, 188]. ONTT showed that the disease recovers with 3 days of intravenous high-dose methylprednisolone and 11 days of oral 1 mg/kg/day prednisone treatment following it. The treatment is more rapid especially in the first 15 days but does not affect long-term visual improvement (Fig. 5.10). Same trial reported that the treatment with oral 1 mg/kg/day prednisone did not show any significant difference with the placebo group, and it was found that there was an increased risk for recurrence of ON surprisingly. Risk of development of MS was reduced in the intravenous methylprednisolone group during the first 2 years, but this benefit diminished over time [188]. A meta-analysis study showed recently corticosteroids have no beneficial effect on final visual acuity [189]. Plasmapheresis for patients with steroid-resistant ON and MNO has found beneficial effect, but there is no level 1 evidence [190, 191]. However, it can be considered as an option for steroid-resistant patients. Studies on the effect of intravenous immunoglobulin treatment are contradictory, and further studies are needed [192, 193].

Beta interferons (IFN-β-1a and IFN-β-1b) and glatiramer acetate have been used for clinically isolated syndrome positive for demyelinating lesions in the MRI, to slow the progression of

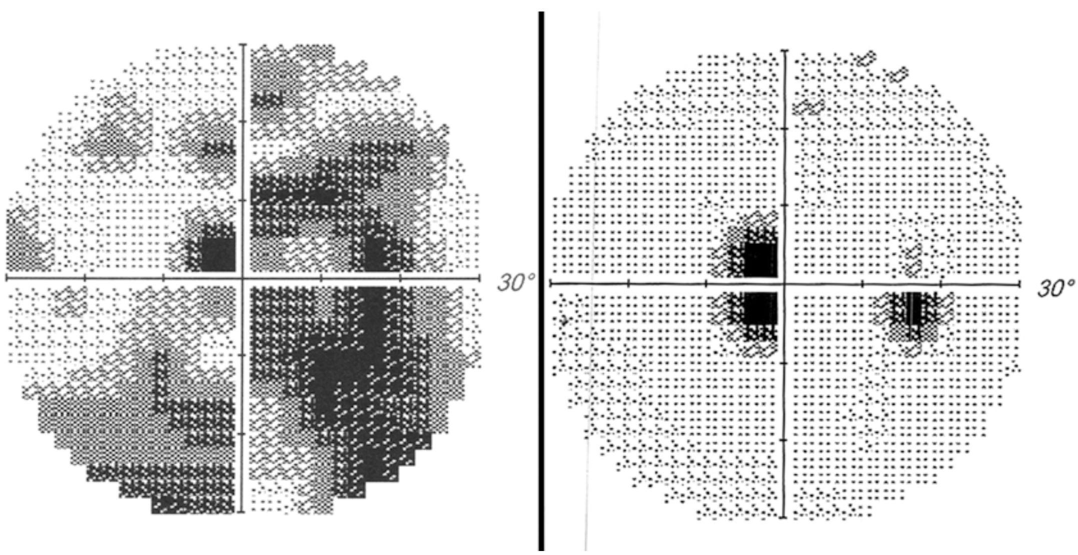

Fig. 5.10 Visual field defect in visual field testing in the patient at Fig. 5.9 showed improvement with intravenous steroid treatment

neurologic deficits. Several clinical trials studied the effect of these drugs on clinically isolated syndromes including isolated optic neuritis [194–197]. The treatment achieved delay of following relapse and conversion to MS the patients. Long-term neurologic disability was relatively mild but did not differ from control groups [198]. In NMO, immune prophylaxis with azathioprine or rituximab is more preferred than beta interferon or glatiramer acetate [199, 200].

5.2.3.2 Anterior Ischemic Optic Neuropathy

Ischemic optic neuropathy is caused by optic nerve blood supply interruption (ION) [201]. The ischemia in optic nerve head supplied by posterior ciliary arteries is called anterior ischemic optic neuropathy (AION) [202]. Pial vascular plexus supplies blood to posterior optic nerve. AION and posterior ischemic optic neuropathy (PION) are the sections of ION according to optic nerve circulation anatomy. These IONs could be arteritic or non-arteritic [203]. Arteritic AION or PION caused by giant cell arteritis is discussed under the topic of giant cell arteritis. The most common type caused by other reasons not satisfactorily revealed yet is non-arteritic AION (NA-AION) or PION.

NA-AION has an estimated annual incidence of 2.3–10.2 per 100,000 individuals ≥50 years of age [204]. There is no gender predisposition. NA-AION occurs in white population than in black or Hispanic people.

Acute optic nerve head ischemia is known as the cause of NA-AION, and the pathogenesis is unclear. Risk factors must be well-understood as it is considered to be a multifactorial disease. Most notable examination finding is small or absent optic nerve head physiologic cup also known as "disc at risk" [205–207]. As optic nerve head swelling is present, it is difficult to see at the acute stage, but examination of the fellow eye can suggest small physiologic cup. It is thought that the small optic disc may induce constriction of posterior ciliary arteries. Diabetes mellitus and hypertension are the most common systemic risk factors [208–211]. Other known systemic risk factors are systemic hypotension, nocturnal hypotension, atherosclerosis, hypercholesterolemia, and sleep apnea [212–218].

Beside systemic risk factors, there are local pathologies affecting blood flow to the optic nerve head [219]. Increased intraocular pressure, vasospasm, chronic optic disc edema, and optic drusen can be included as local risk factors. Some drugs are also accused of causing NA-ION, including phosphodiesterase type 5 inhibitors used for erectile dysfunction, amiodarone, and vasoconstricting drugs such as nasal decongestants [220–225].

NA-AION presents with sudden, painless visual loss [226]. Loss of vision is generally unilateral, accompanied by a loss of visual field (Fig. 5.11). Afferent pupillary defect is usually present. Optic disc is swollen and hyperemic at fundus examination, and small physiologic cup can be seen in the fellow eye. There may be segmental or diffused optic disc edema.

First of all, C-reactive peptide (CRP) and erythrocyte sedimentation rate (ESR) measurements should be performed for the distinction of NA-AION and A-AION [227]. Increased levels of ESR and CRP should suggest A-AION proven with temporal artery biopsy. Optical coherence tomography imaging for retinal nerve fiber layer thickness can be useful for acute phase optic disc edema and chronic stage atrophy [228–230].

Many treatments have been studied before, but no proven treatment has been found for NA-AION. Optic nerve sheath decompression was shown not to be useful for treatment by Ischemic Optic Neuropathy Decompression Trial (IONDT) [231]. Aspirin therapy used in control group did not have a beneficial visual acuity effect and did not reduce NA-AION risk in the fellow eye within long-term results [232–234]. Intravitreal anti-VEGFs and corticosteroids have no effect on visual improvement but are helpful for optic disc edema reduction [235–237]. Optic nerve head ischemia is known to cause NA-AION; for this reason, intravitreal injections can be harmful due to increasing intraocular pressure.

Use of systemic corticosteroids seems to be beneficial. Hayreh et al. reported that visual acuity and visual field improvement up to 6 months are provided through early treatment of NA-AION

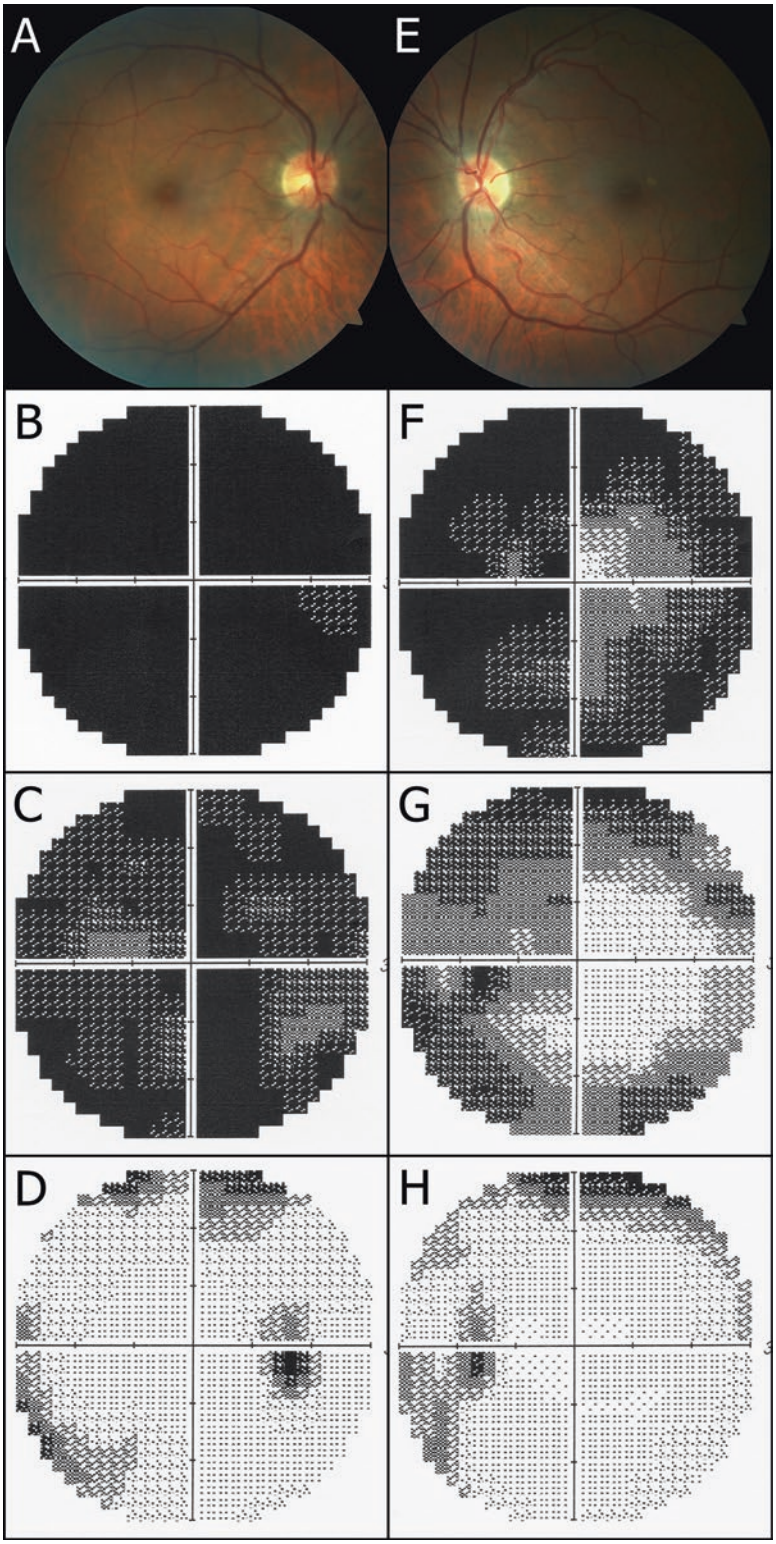

Fig. 5.11 A 62-year-old patient who had regular intake of sildenafil, presented with visual loss starting at 1-week interval. Best corrected visual acuity was CF 3 mt for the right eye and 0.16 for the left eye. Methylprednisolone 1 g/day was used intravenously and was followed by oral prednisone 1 mg/kg/day. (**a** and **e**) No pathology was seen in retinal fundus photography. (**b** and **f**) Severe visual field loss in both eyes at the time of admission was seen in 30–2 Humphrey visual field testing. (**c**, **d**, **g**, and **h**) One month after the last steroid intravenous administration, visual acuity for the right eye had increased to 0.9 and to 1.0 for the left eye. Visual field loss was resolved at the same time

with 80 mg prednisone daily for 2 weeks, tapering it down to 70 mg for 5 days, 60 mg for 5 days, and then 5 mg every 5 days [238]. Prospective and randomized clinical studies are needed to investigate the therapeutic effects of systemic corticosteroids with these results. Other medications including dabigatran, pentoxifylline, memantine, and topical brimonidine were not effective for visual acuity and visual field improvement [239–243]. Hyperbaric oxygen therapy has also no beneficial effect [244].

Long-term results of the NA-AION vary. Studies showed a spontaneous recovery of three Snellen lines or more in 13–43% [234, 245, 246]. Although there is no any proven treatment, patients should be advised to reduce risk factors. It is essential for reducing NA-AION development risk in the fellow eye and recurrence in the same eye.

5.2.3.3 Giant Cell Arteritis

Giant cell arteritis (GCA), temporal arteritis in other words, is a systemic granulomatous medium- to large-sized vessel vasculitis [247]. GCA is a potentially sight-threatening ophthalmic emergency. Involving the ophthalmic artery, GCA reduces blood supply to the eye which may result irreversible visual loss [248]. The most seen ocular manifestation is ischemic optic neuropathy.

Occurring mostly in elder patients >50 years of age, its incidence increases between the ages 70–80 [248]. Scandinavian or Northern European people and women are more commonly affected [249, 250].

Activation of vascular dendritic cells that are residing in the vessel walls is the first step of the pathophysiology [251] Activated dendritic cells recruit T cells which produce interferon-γ. Interferon-γ targets monocytes and macrophages which form giant cell formation. In addition, there is also evidence of local vascular cell dysfunction. Endothelial cells provide access for immune cells and produce endothelin which is a proinflammatory vasoactive peptide. In GCA, vascular smooth muscle cells transform into a secretory cell that are involved in the synthesis of matrix metalloproteinases. Outside of the vessel wall, platelets and leukocytes contribute with producing prothrombotic mediators.

The most common clinical presentation of GCA in elderly patients is vision loss with headache [252]. Jaw claudication and scalp tenderness are very important symptoms that have a strong relationship with GCA [253]. Fatigue, fever, anorexia, and weight loss and similar nonspecific symptoms may be seen as disease-caused inflammation symptoms. Vision loss is generally unilateral, but there are some cases with bilateral loss of vision, even though in some cases vision may be normal at the time of diagnosis.

GCA has various ocular manifestations (Figs. 5.12 and 5.13). Clinician should be aware of the ocular presentation with associated symptoms. With its branches as anterior (AION) and posterior (PION) ischemic optic neuropathy, ischemic optic neuropathy is the most common vision loss reason [248, 254], and arteritic anterior ischemic optic neuropathy (A-AION) is its most common form. The cause is the occlusion of short posterior ciliary arteries. Visual field defects and abrupt vision loss are the complaints of the patients. When arteritic posterior ischemic optic neuropathy occurs, optic nerve can look normal with loss of vision. Choroidal ischemia, central retinal artery occlusion, ocular ischemic syndrome, anterior segment ischemia, scleritis,

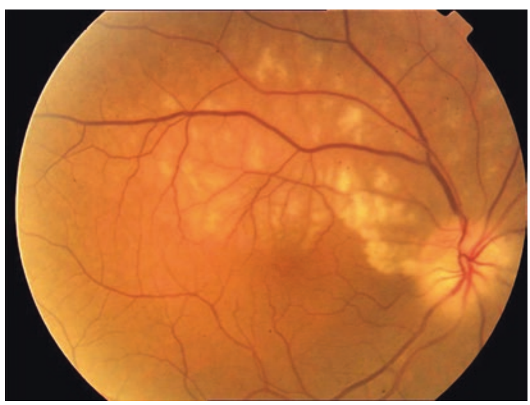

Fig. 5.12 Color fundus photo of a 74-year-old male patient with visual loss (VA: hand movements) and temporal hemifacial pain complaints. RAPD was present at onset. Optic disc pallor and edema and retinal edema were prominent findings. LAB. Findings; CRP: 74, ESR: 75 mm/h

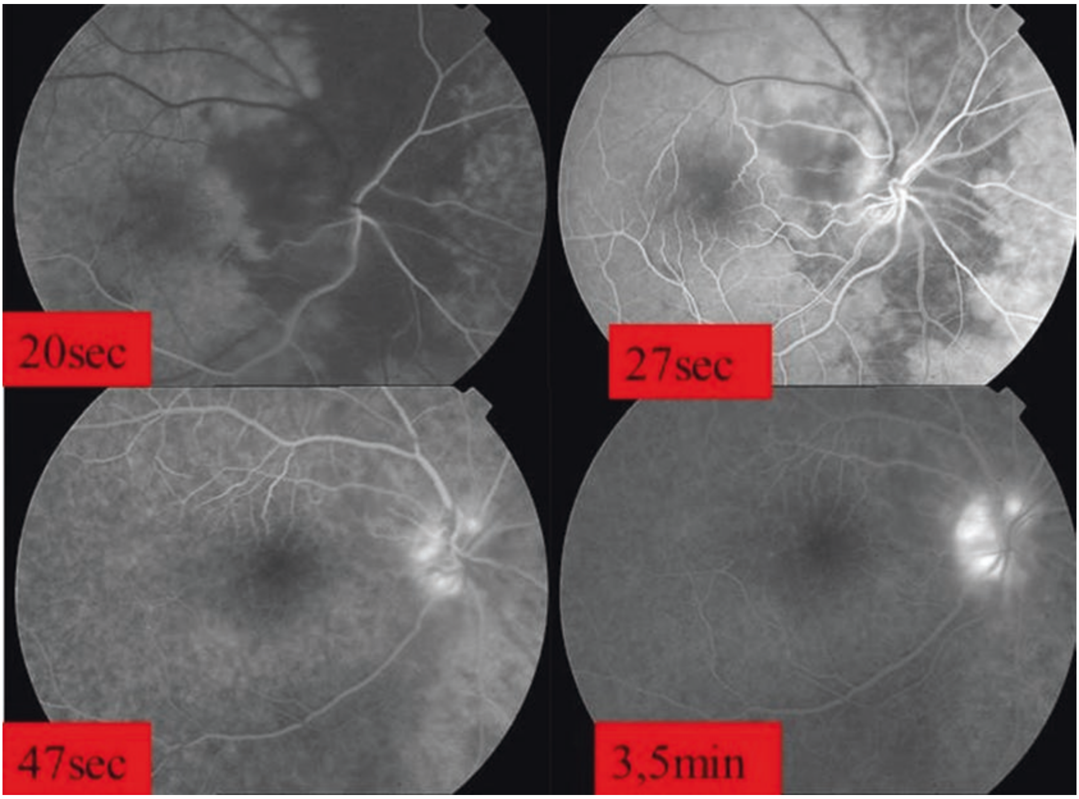

Fig. 5.13 Fluorescein angiography of the patient in Fig. 5.12 reveals marked choroidal nonperfusion as well as delayed slow retinal arteriolar perfusion and late optic disc staining

peripheral ulcerative keratitis, and ophthalmoplegia are the other ocular manifestations of GCA [255–265].

There is a significant association with GCA and polymyalgia rheumatic [266]. They are separate syndromes, but polymyalgia rheumatica can be seen at almost 50% of patients with GCA [267]. Both diseases have common risk factors and pathogenic abnormalities. Optic disc swelling and pallor are the typical findings at acute phase of the disease. Optic atrophy develops at the chronic stage.

Clinical findings and symptoms constitute the basis of GCA diagnosis. American College of Rheumatology states that GCA diagnosis requires three or more of five major criteria: age of ≥50 years, new-onset headache, clinical temporal artery abnormality, elevated erythrocyte sedimentation rate (ESR) (≥50 mm/h), and positive temporal artery biopsy [268]. Although the gold standard is temporal artery biopsy, laboratory tests may also be helpful (Fig. 5.14). C-reactive protein (CRP) can be found elevated as ESR. CRP and ESR can be found normal in a group of patients [269]. Full blood count is a useful test for detecting elevated platelets. Perivascular hypoechoic abnormality (halo sign) is the most specific finding of color Doppler ultrasonography [270].

Patients with GCA or A-AION, whether proven or suspected, should be treated immediately. Aims of the treatment are to prevent fellow eye visual loss and systemic vasculitis complication [271]. High-dose systemic corticosteroids are used to control inflammation. Prolonged treatment with slow taper down is recommended for GCA [272]. There is not a consensus for the initial dose of corticosteroids, but 1 mg/kg/day prednisone is generally enough for responding [253]. Higher dose is needed for the patients with

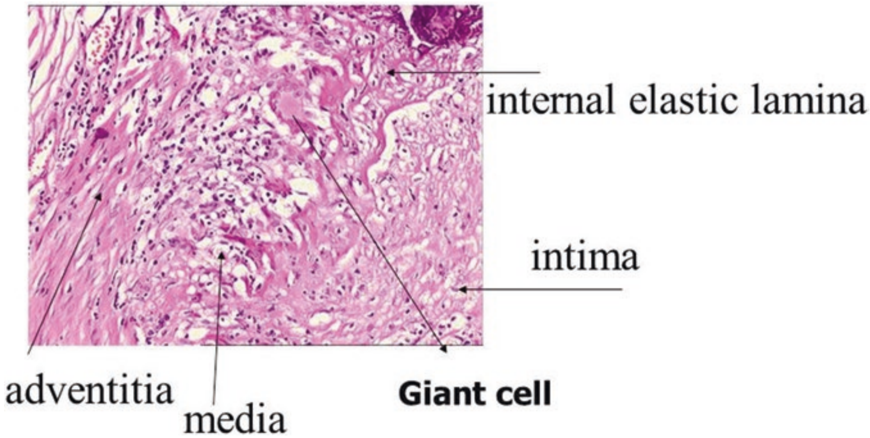

Fig. 5.14 Histopathologic section of temporal artery biopsy reveals thickening and presence of inflammatory cells at all vessel layers. Giant cells are present as one of the distinct markers of the disease

visual and neurologic symptoms such as 1–1.5 mg/kg/day of prednisone [273]. Alternative treatment for patients with high visual loss risk is high-dose intravenous methylprednisolone (1 gr per day for 3 to 5 days) [274]. High-dose corticosteroids are effective, but clinician must be aware of possible side effects [275]. In patients with serious corticosteroid side effect or steroid-resistant disease, corticosteroid-sparing treatment modalities are available. These treatments include methotrexate, infliximab, etanercept, adalimumab, leflunomide, anakinra, tocilizumab, cyclophosphamide, and rituximab [253, 271]. The efficacy of these drugs is not proven; therefore, use of the steroid-sparing agents remains controversial.

Patients should be followed up at close intervals during the first month of treatment and then every 3 months during the first year, with consecutive measurement of ESR, CRP, electrolytes, full blood count, and fasting glucose. Corticosteroid treatment duration should be for months to years and titrated according to the resolution of the systemic and visual symptoms and ESR and CRP levels.

5.2.4 Vitreous Hemorrhage

By definition, vitreous hemorrhage (VH) is extravasation through the vitreous humor. Hemorrhage into Cloquet's canal is accepted in the definition of VH.

The estimated annual incidence of VH is 7 in 100,000 [276]. Possible pathological mechanisms causing vitreous hemorrhage include hemorrhage from an abnormal retinal vessel, rupture of normal retinal vessel due to trauma or posterior vitreous detachment (PVD), and spread of blood from an adjacent source. Most common cause of VH is proliferative diabetic retinopathy (6–54%), followed by trauma (12–18.8%), retinal tear (11.4–44%), PVD without retinal tear (3.7–11.7%), and retinal vein occlusion (3.5–16%) [277]. In young people, the most common VH cause is trauma [278]. Other causes are sickle cell retinopathy, retinal macroaneurysm, age-related macular degeneration, and Terson's syndrome [279]. Secondary to the ocular surgery, retinal vascular pathologies tumors, inflammation, coagulopathies, and Valsalva maneuver are other pathologies causing VH.

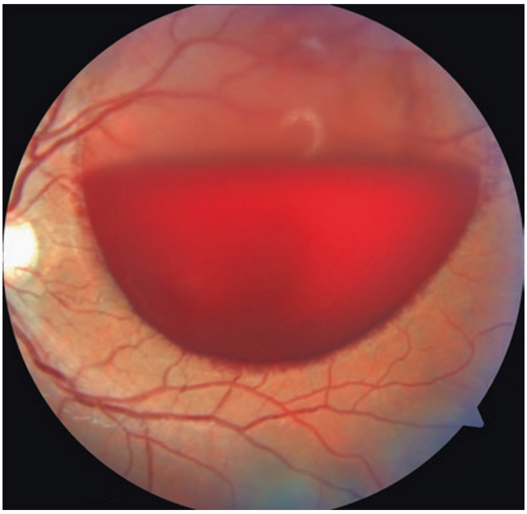

Fig. 5.15 Patient with subhyaloid hemorrhage. See the boat-shaped hemorrhage in front of the fovea

Sudden loss of vision is the usual presentation of VH. Floaters, blurry vision, and perception of shadows and cobwebs are common symptoms before loss of vision. Visual loss is usually painless, but pain may occur due to underlying pathology. Slit-lamp examination, gonioscopy, and intraocular pressure measurement should be covered in the complete examination and fundus examination if possible, and B-scan ultrasonography should be performed in all patients. Blood cells may be seen behind the lens at slit-lamp microscopy.

Fundus reflex may not be seen on ophthalmoscopy in patients with dispersed hemorrhage into the vitreous humor. Retinal examination can be performed in case of nondispersed hemorrhage. Hemorrhage trapped between posterior hyaloid and internal limiting membrane on the macula known as subhyaloid hemorrhage is usually seen as boat-shaped (Fig. 5.15) [280]. Subinternal limiting membrane hemorrhage which may be caused by Terson's syndrome, shaken baby syndrome, Valsalva retinopathy, and retinal macroaneurysm is similar to subhyaloid hemorrhage, but the blood does not move with the head position [281–283]. If complete view of retina is covered by hemorrhage, B-scan ultrasonography should be performed to detect possible retinal detachment, intraocular tumor, or foreign body. Fundus fluorescein angiography, magnetic resonance imaging, computerized tomography, and blood testing should be performed according to the suspected etiologies.

Hemorrhage into the vitreous humor clears at a rate of approximately 1% per day which results in rapid formation of a clot (Fig. 5.16) [277]. On the other hand, hemorrhage localized in anterior or posterior hyaloid doesn't clot [284]. The blood is cleared rapidly in vitrectomized and syneretic eyes. Erythrocytes in the hemorrhage exit the eye through the trabecular meshwork and undergo hemolysis. It may persist for months, especially in young people with well-formed vitreous. If hemorrhage is not cleared from the vitreous within a year, complications such as hemosiderosis bulbi, proliferative vitreoretinopathy, ghost cell glaucoma, and hemolytic glaucoma may occur [277].

Prognosis and the choice of treatment vary according to the underlying disease. Patients with VH should be examined every day for 2–5 days to be able to rule retinal detachment or tear out and then every 1–2 weeks to provide spontaneous resolving. Vitrectomy should be performed as soon as possible if the pathology is retinal tear of detachment [285]. If the retina is attached in the ultrasonography, it can be treated conservatively for 1 or 2 months except in the presence of iris or angle neovascularization due to proliferative retinal disease [286]. Treatment of anterior segment neovascularization is needed in panretinal laser photocoagulation (PRP), and it can be possible with only early vitrectomy.

If posterior pole of the retina is covered by hemorrhage, resting in a bed with 30–45° elevated head may provide a view of the superior peripheral fundus allowing the blood to settle inferiorly. Aspirin and any forms of anticoagulation are generally not discontinued during the observation [287]. When the retina can be visualized, the underlying cause can be determined and treatment can be planned. If the cause is retinal neovascularization, PRP and anti-VEGF injections can be performed [288].

Vitrectomy is indicated for dense or nonresolving VH, new-onset neovascularization, and ghost cell glaucoma [289]. Nd:YAG laser hya-

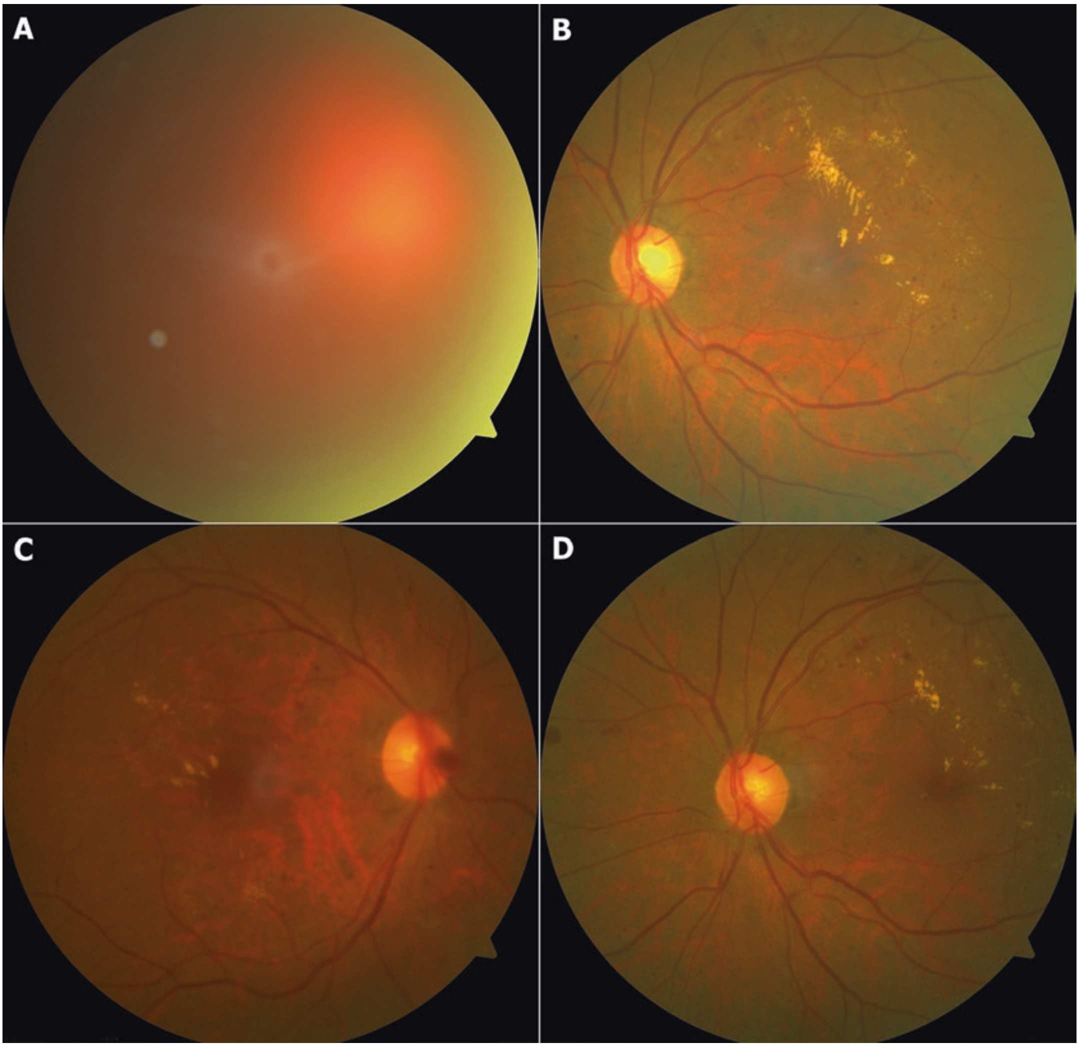

Fig. 5.16 Diabetic patient with vitreous hemorrhage at the right eye. (**a**) Bleeding into the vitreous covers the view of the fundus. (**b**) Fundus photography of the left eye. Hard exudates, microaneurysms, and dot-blot hemorrhages draw attention at the posterior pole. (**c**) Three months after A. Hemorrhage was cleared from the vitreous. Optic disc neovascularization was noticed and panretinal laser photocoagulation was planned. (**d**) Three months after (**b**). Exudates and microaneurysms regressed with strict blood glucose control

loidotomy can be performed for subhyaloid and subinternal limiting membrane hemorrhage to get early visual recovery (Fig. 5.17) [280, 290].

5.2.5 Rhegmatogenous Retinal Detachment

The act of separating neurosensory retina and underlying retinal pigment epithelium and choroid is called retinal detachment [291]. Passively, the detachment can occur due to liquefied vitreous accumulation between these two layers from a retina break or actively due to diabetic traction retinal detachment or similar retinal traction [292]. Retinal detachment causes ischemia in neurosensory retina and rapid, progressive photoreceptor degeneration (Fig. 5.18). Late referral to the hospital or treatment is the main reason for persistent vision loss.

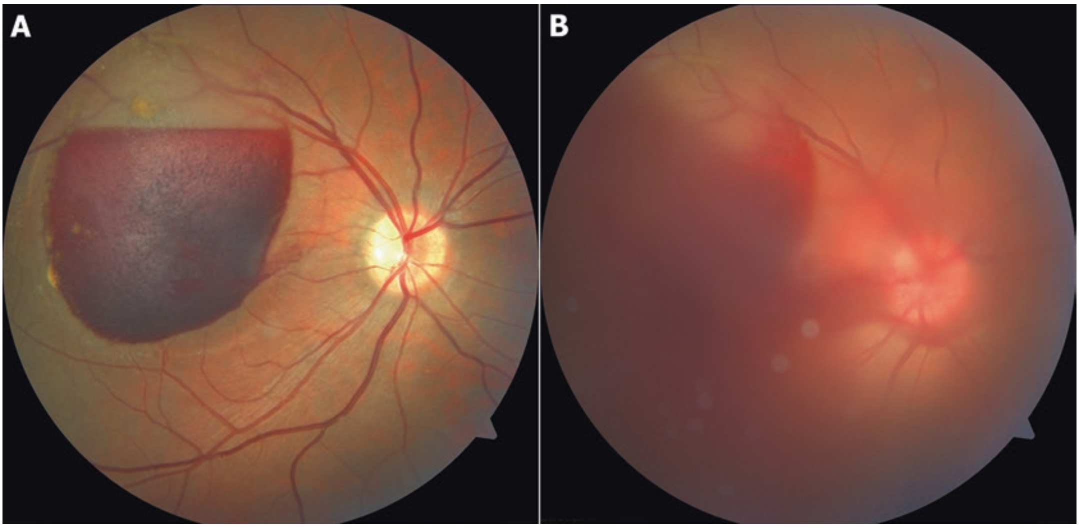

Fig. 5.17 Treatment of subhyaloid hemorrhage with Nd:YAG laser. (**a**) Subhyaloid hemorrhage at the premacular area. (**b**) Hyaloidotomy with Nd:YAG laser caused to spread blood into the vitreous

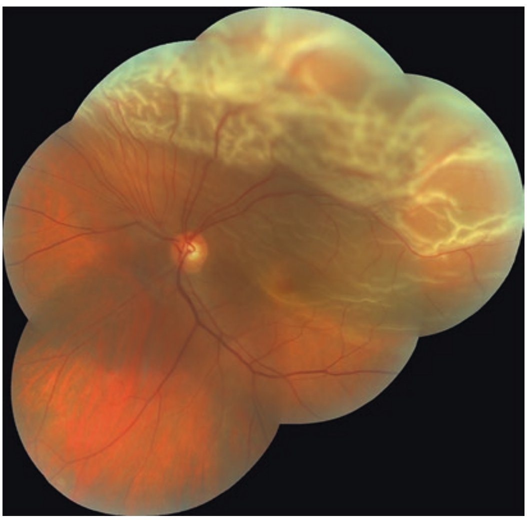

Fig. 5.18 Patient with macula-off rhegmatogenous retinal detachment

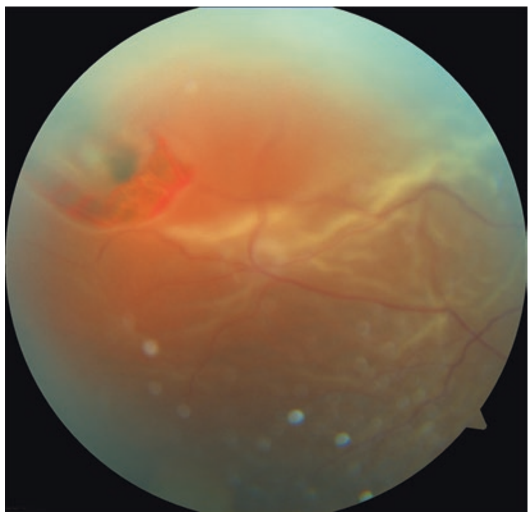

Fig. 5.19 Horseshoe-shaped retinal tear at the upper temporal part of the retina

Rhegmatogenous retinal detachment is the most common retinal detachment type [291]. Full-thickness retinal tear or hole causes retinal detachment (Fig. 5.19). Rhegmatogenous retinal detachment occurs in approximately between 6.3 and 17.9 in 100,000 persons per year [293]. Myopia constitutes the most important nontraumatic rhegmatogenous retinal detachment risk factor, and cataract surgery, posterior vitreous detachment (PVD), lattice degeneration, retinal tears, family history, and glaucoma are other risk factors [294].

PVD is the most common cause of retinal holes and tears [295]. Although asymptomatic breaks are more common, symptomatic breaks are more likely to cause retinal detachment. Rhegmatogenous retinal detachment may develop in approximately 21.7% of patients with

a full-thickness horseshoe retinal tear in a symptomatic vitreous detachment setting [296]. Ocular trauma also may develop a full-thickness retinal break or dialysis [297].

Patients with rhegmatogenous detachment usually suffer from an increasing number of gloaters or flashes in only one eye and similar acute PVD symptoms. Avulsion of small retinal vessel may result in vitreous hemorrhage. Shower of black spots may occur in patients with vitreous hemorrhage. Retinal detachment progression rate depends on retinal break size and location and eye movements. Patients complain of a sensation that "curtain is falling" if the accumulation of subretinal fluid progresses posterior to the equator. When subretinal fluid passes beneath the macula, central visual acuity is lost. Patients do not usually notice any visual symptoms until the macula detached.

Patients with sudden onset of floaters, or flashes, who present to primary care, should be referred to an ophthalmologist if vision loss found. All patients should undergo slit-lamp biomicroscopy and fundus examination. Pigmented vitreous cells behind the lens called "tobacco dust" can be seen on the anterior segment examination. Binocular stereoscopic examination of the entire retina must be performed using an indirect ophthalmoscope with scleral indentation of the peripheral retina to detect retinal breaks associated with rhegmatogenous retinal detachment. Pigment epithelial and choroidal detail cannot be seen beneath the elevated neurosensorial retina in the fundus examination. In eyes with opaque media, such as cataract, corneal scarring, or vitreous hemorrhage, the presence of a retinal detachment is usually evaluated by ultrasonography. Clinician must perform examination of the fellow eye as there is a relatively high rate of retinal tears or detachments [293].

Rhegmatogenous retinal detachments should be differentiated from serous or tractional retinal detachments and retinoschisis as well as choroidal lesions that elevate the overlying retina and intravitreal pathology which simulates an elevated retina.

Patients with symptomatic PVD do not require any treatment if there is no retinal tear or hole.

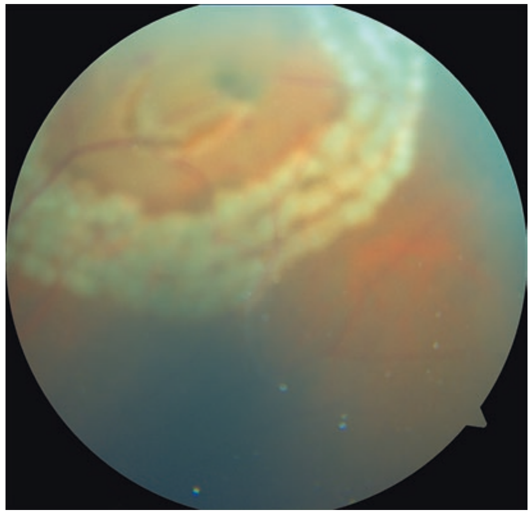

Fig. 5.20 Treatment of a retinal tear. Laser spots can be seen around the retinal tear

Patients must be educated about alert symptoms and should be seen in follow-up at about 3 months. Patients with flashes or retinal bleeding should be seen earlier, like 1 or 2 months. There is no need of any limitation on activities. If symptomatic retinal tear or hole is present, the patient will benefit from laser photocoagulation or cryotherapy [298]. It may reduce the risk of rhegmatogenous retinal detachment but not reset (Fig. 5.20). Laser photocoagulation can be performed by using the slit-lamp biomicroscope or indirect ophthalmoscope depending on the location of retinal tear or hole. Asymptomatic retinal tear or hole does not require prophylactic laser photocoagulation or cryotherapy because the risk of rhegmatogenous retinal detachment is already low [299].

Small, peripheral, asymptomatic retinal detachments can be treated with laser photocoagulation or cryotherapy [300]. Other than that interventional therapies including pneumatic retinopexy, scleral buckle placement, or pars plana vitrectomy is required.

Pneumatic retinopexy is a relatively cheap and efficient treatment for selected rhegmatogenous retinal detachments [301]. It can be performed in the office with topical anesthesia and needed strict head positioning after the procedure. A single break smaller than 1 clock hour in superior 8

clock hours of the retina or a group of small breaks within 1 clock hour is the main pneumatic retinopexy indication. Intravitreal gas bubble (0.6 ml of sulfur hexafluoride-SF6 or 0.3 ml of perflouoroprane-C3F8) is used to reattach the retina and retinal tear sealed by laser photocoagulation 24–28 h after gas injection. Failure is usually associated with inferior retinal tears or development of new tears. In cases of failure, most patients are treated with surgery including scleral buckle or pars plana vitrectomy [302].

Scleral buckling relieves the radial vitreous traction. In addition, buckling material displaces some subretinal fluid away, reposing the retina to the RPE [303]. Scleral buckling surgery can be performed in a large group of retinal detachments except patients with posterior breaks, giant retinal tear, and patients in whom placement of the buckling material is too difficult. General complications of the procedure are myopic refractive change, motility disturbances, vitreous or retinal incarceration, suprachoroidal hemorrhage, and migration of buckling materials [304]. Scleral buckling surgery provides successful retinal reattachment approximately 80–90% with single surgery [305, 306]. Most patients undergo vitrectomy if scleral buckling fails.

There is an increase in the application of primary pars plana vitrectomy, especially in pseudophakic patients [307]. Removal of the vitreous with pars plana vitrectomy eliminates the traction over the retinal tear. Improved instruments and techniques increased the use of PPV, but it may be a more expensive procedure other than surgeries. The surgery generally needs a tamponade (SF6, C3F8, or silicone oil) with a body or head position (Fig. 5.21). Most common complications are cataract and increased intraocular pressure. The procedure can be combined with scleral buckling or cataract surgery.

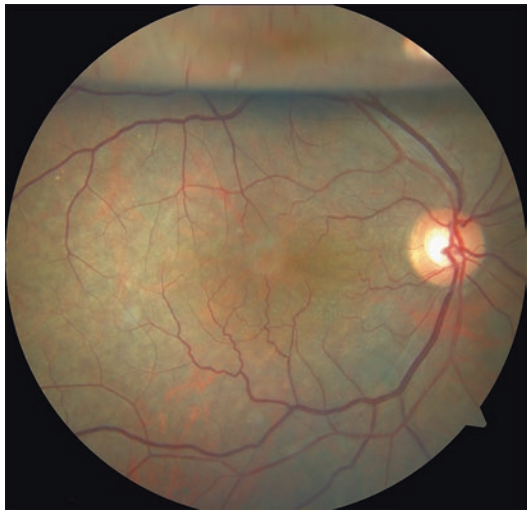

Fig. 5.21 A patient with retinal detachment who underwent pars plana vitrectomy. SF6 gas was used as tamponade and gas bubble can be seen at the superior part of the retina

5.2.6 Stroke

Ischemic disease in anterior or posterior cerebral vascular system may cause loss of vision. Ischemic stroke refers to a neurological dysfunction that lasts more than 24 h due to ischemia of focal cerebral, spinal, or retinal cell death [308]. Approximately 5–10% of ischemic strokes is caused by the posterior cerebral artery (PCA) or its branches [309]. Embolism is found to be the most common pathology in posterior circulation stroke which originates from atheromatous vertebral arteries, the aorta, or the heart [58].

Patients with PCA infarct may present with the symptoms of acute vision loss, paresthesia, dizziness, nausea, confusion, headache, limb weakness, and language dysfunction [15]. Associated brainstem infarctions cause more complex neurologic deficits. Ischemia of thalamus presents contralateral face and limb sensory loss. It is important to recognize stroke when visual defects occur with neurologic symptoms. Patients may not be aware of visual loss or may not be able to define their change in vision well. Most common visual disturbance is homonymous hemianopia caused by ischemia in the contralateral occipital lobe [310]. Sparing of the central 2°–10° of the visual field due to dual blood supply to the posterior occipital lobe is commonly found with occipital lobe ischemia. Although mortality from PCA stroke is low, morbidity is relatively high due to associated brainstem infarction [311].

Complete neurologic, cardiologic, and vascular examination should be performed in all patients with posterior circulation stroke. Full blood count, serum glucose, electrolytes, creatinine, prothrombin time, activated partial thromboplastin time, and international normalized ratio should be performed at referral to evaluate whether the patient is a candidate for acute stroke treatment and possible stroke. The most important embolism source is cardiac, and therefore electrocardiogram, echocardiogram, and cardiac monitoring are required.

Computerized tomography (CT) scanning, magnetic resonance imaging (MRI), CT angiography (CTA), MR angiography (MRA), and such imaging methods are extremely important in the diagnosis and evaluation of PCA strokes. CT scanning is sensitive in diagnosis of intracranial hemorrhage [312]. MRI including diffusion-weighted images demonstrates acute ischemia much earlier and better than CT scanning (Fig. 5.22) [313]. CTA or MRA can detect extracranial or intracranial vascular pathologies such as stenosis and embolism.

Digital subtraction angiography (DSA) is the gold standard method, but it is invasive and has a risk of procedure-related morbidity [314]. However, DSA is necessary to perform endovascular treatment.

Thrombolysis with intravenous tissue plasminogen activator (tPA) is effective in the first 3 h of event [315, 316]. But the procedure is performed rarely because patients do not consider acute loss of vision as a potential emergency and therefore they do not refer to emergency room. Intracerebral hemorrhage is a very severe complication of thrombolysis; for this reason, there are rigid guidelines for administering tPA. There is no class I evidence about endovascular therapies for PCA stroke, but it can be performed if the patient fails to respond to medical management [317]. Anticoagulant and antiplatelet therapies and rehabilitation should be planned for the long-term follow-up.

5.2.7 Hysteria

The term of hysteria refers to psychogenic blindness or conversion disorder. Loss of vision without any ocular, neurological, or vascular pathology should suggest the diagnosis of

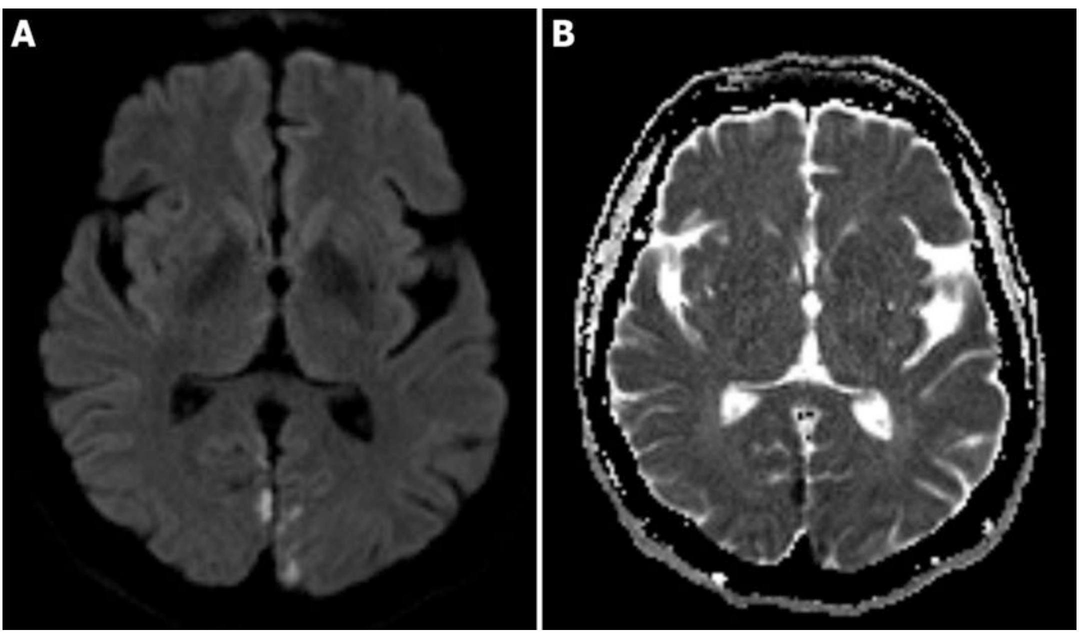

Fig. 5.22 MRI scan demonstrating acute ischaemic infarcts invoking parafalcian bilateral occipital region as hyperintensity signal in restricted diffuison weighed imaging (**a**) with corresponding hypointensity signals in apparent diffusion coefficient (**b**)

psychogenic blindness [318]. It is more common among younger age and women. Loss of vision occurs after stressful events.

Patients generally complain about a reduction of visual acuity with or without loss of visual field. The diagnosis should be made after complete ophthalmologic and neurologic examination and laboratory and imaging tests. Optokinetic stimulation testing for nystagmus can be done to reveal intact vision [319]. Electrophysiological tests such as visual evoked potentials may help to prove intact visual pathways. In case of the diagnosis of hysteria, psychiatry consultation should be done for appropriate treatment.

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6 Acute Visual Field Impairment

Bo Huang and Suxia Li

Abstract

Acute visual field loss is a clinical sign that is frequently encountered in the emergency room. The visual field loss could be caused by a variety of ocular as well as neurological disease processes. Successful diagnosis of visual field loss cases requires careful differential analysis of a wide variety of possibilities, complete examinations of medical and ocular history, and comprehensive ophthalmic examinations. Ancillary tests play a major role in assisting the correct diagnosis of these diseases. Major causes of acute visual field loss are discussed in this chapter.

Keywords

Branch retinal artery occlusion (BRAO) · Central retinal artery occlusion (CRAO) · Branch retinal vein occlusion (BRVO) · Central retinal vein occlusion (CRVO) · Retinal detachment · Optic neuropathy · Optic neuritis · Anterior ischemic optic neuropathy · Neuroretinitis

6.1 Branch Retinal Artery Obstruction

Branch retinal artery obstruction (BRAO) is a retinal vascular disorder that is often associated with systemic diseases. When dealing with this disease, it is crucial for clinicians to determine the possible sources of obstruction. The diagnosis and systemic evaluation of these patients are critical.

6.1.1 Epidemiology and Pathogenesis

Branch retinal artery obstruction is a rare event, even less common than central retinal artery obstruction (CRAO). It, however, more commonly occurred in younger patients than CRAO [1]. Men are more affected than women by a 2:1 ratio. The mean age of affected patients is 60 years, with the great majority of patients in the sixth or seventh decade of life. The right eye

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(60%) is affected more commonly than the left (40%), which likely reflects the greater possibility of cardiac or aortic emboli traveling to the right carotid artery [2].

A majority of the BRAOs are secondary to emboli blockage of the retinal circulation [2–4]. In most cases, the emboli are visible in the arterial tree, and they may originate at any point in the proximal circulation from the heart to the ophthalmic artery. The risk factors include predisposing family history, hypertension, elevated lipid levels, cigarette smoking, and diabetes mellitus.

The three main types of retinal emboli are:

- Cholesterol (Hollenhorst plaque)
- Platelet-fibrin
- Calcific

These retinal emboli have their own characteristic appearances. Cholesterol emboli are typically formed from atheromatous plaques of the ipsilateral carotid artery system. They appear yellow orange in color, refractile, and globular or rectangular in shape. Platelet-fibrin emboli are usually associated with carotid or cardiac thromboses, and they appear as long, smooth, white-colored, intra-arterial plugs. Calcific emboli are solid, white, nonrefractile plugs associated with calcification of heart valves or the aorta.

Other less common embolic types include tumor cells from atrial myxoma [5] or a systemic metastasis, septic emboli associated with septicemia or endocarditis, fat emboli associated with large bone fractures, emboli dislodged during angioplasty or angiography, and depot drug preparations from intra-arterial injections around the eye or face.

Local ocular conditions rarely produce BRAO. These include inflammatory diseases, such as toxoplasmosis or acute retinal necrosis, or structural entities, such as optic disc drusen or prepapillary arterial loops [2, 3].

Systemic hematological diseases may induce isolated or multiple recurrent branch retinal artery obstruction [6, 7]. Systemic vasculitides, such as polyarteritis nodosa or local vasculitis associated with varicella infection, can also be associated with branch retinal artery obstruction. Oral contraceptive use and cigarette smoking have been implicated as possible risk factors, especially in young, otherwise healthy women [1, 8].

6.1.2 Ocular Manifestations

A characteristic ocular history of BRAO is acute painless loss of vision in the visual field corresponding to the territory of the obstructed artery. Patients can typically relate to the precise time and extent of visual loss. In some cases, amaurosis fugax precedes artery obstruction in the setting of carotid disease.

On examination, the patient's central acuity is unaffected in about 50% of cases. A relative afferent pupillary defect can occur depending on the extent of retinal involvement.

A fundus examination will reveal retinal whitening that corresponds to the areas of ischemia. The ischemic area stops at adjacent retinal veins, as these vessels mark the extent of the territory of the retinal arteries (Fig. 6.1). The clinicians can often identify the presence of retinal emboli in over two thirds of BRAOs. Flame hemorrhages and cotton-wool spots can also be seen on fundus exam.

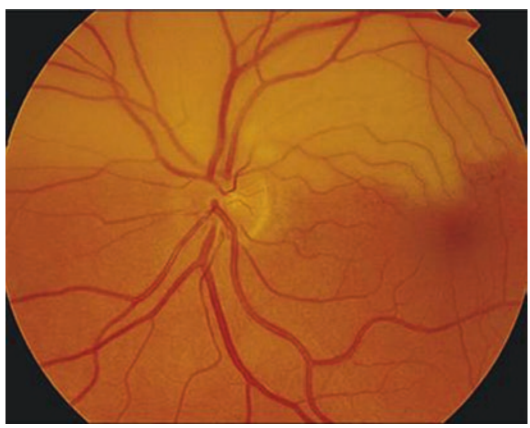


Fig. 6.1 Superior hemispheric branch retinal artery obstruction. Note the superior half of the retina was affected

Young, healthy patients with Susac's syndrome, a rare disorder with microangiopathy of the central nervous system, can develop multiple, recurrent, bilateral branch retinal artery obstruction. Some of the patients also manifest vestibuloauditory symptoms [9, 10].

After the resolution of retinal ischemia, the retina may return to normal function. However, a loss of the nerve fiber layer in the affected area may be apparent. Localized sheathing of the arteriole is common, and arteriolar collaterals on the optic disc or at the site of obstruction may develop.

6.1.3 Diagnosis and Ancillary Testing

Fluorescein angiography reveals an abrupt blockage of dye at the site of the obstruction and distally. Fluorescein filling in the adjacent retinal veins is slow to absent, and late staining or leakage from the embolus site may occur. Optical coherence tomography (OCT) shows a thickening of the inner retina in the territory of the obstructed artery. The corresponding inner retina will be severely thinned over time.

Visual field testing will reveal the extent of visual field loss to the corresponding blockage area.

6.1.4 Differential Diagnosis

The differential diagnosis of branch retinal artery obstruction is shown in Table 6.1.

Table 6.1 Differential diagnosis of branch retinal artery obstruction

Cotton-wool spot(s)
Central retinal artery obstruction
Cilioretinal artery obstruction
Retinal astrocytoma
Inflammatory or infectious retinitis

6.1.5 Systemic Associations

The main systemic associations of branch retinal artery obstruction are the carotid arteries or the heart in many cases. Other rare systemic conditions include amniotic fluid embolism, pancreatitis, sickle cell disease, homocystinuria, and Kawasaki disease. Young patients, especially those who have multiple or recurrent branch retinal artery obstruction, should be evaluated for systemic clotting abnormalities such as protein S deficiency, protein C deficiency, antithrombin III deficiency, platelet abnormalities ("sticky platelet syndrome"), and antiphospholipid antibodies. Branch retinal artery obstruction is usually not associated with temporal arteritis [11].

6.1.5.1 Pathology

Early, coagulative necrosis of the inner layers of the neural retina with edema of the neuronal cells occurs during the first few hours after arterial occlusion and becomes maximal within 24 h. The intracellular swelling accounts for the gray, retinal opacity seen clinically. When coagulative necrosis is small and localized, it appears as a cotton-wool spot, which is the microinfarct of the nerve fiber layer of the neural retina. The cytoid body observed microscopically (Fig. 6.2) is a swollen, interrupted axon in the neural retinal nerve fiber layer.

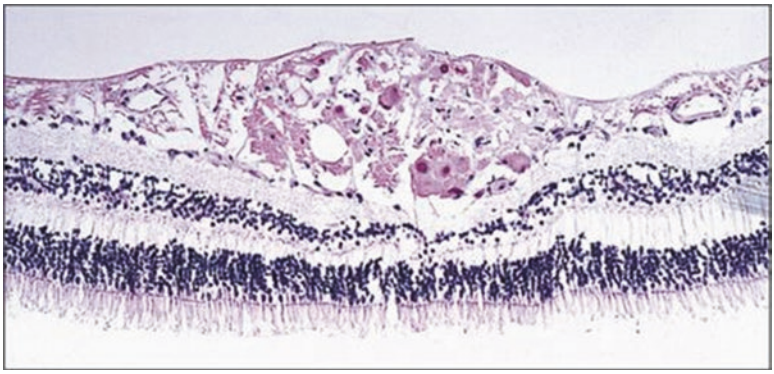
The outer half of the neural retina is well preserved. The inner half of the neural retina, however, becomes "homogenized" into a diffuse, relatively acellular zone with thick-walled retinal blood vessels.

6.1.5.2 Treatment

There is no definitive treatment for branch retinal artery obstruction. Ocular massage and paracentesis have shown to be successful in dislodging an embolus. Laser photocoagulation has been employed to "melt" an embolus, but with no improvement in visual outcome [12].

Hyperbaric oxygen therapy has also been reported in selected cases to improve the visual loss associated with multiple branch retinal artery obstruction in Susac's syndrome [13].

Fig. 6.2 Cytoid body formation in neural retinal nerve fiber layer



6.1.6 Course and Outcome

Most patients remain with a fixed visual field defect but intact central acuity. About 80% of eyes recover to 20/40 (6/12) or better central acuity. Retinal and iris neovascularization are uncommon [2].

6.1.7 Ophthalmic Artery Obstruction

Ophthalmic artery obstruction is the simultaneous obstruction of both the retinal and choroidal circulations.

Ophthalmic artery obstructions can be differentiated clinically from central retinal artery obstruction by the following features: [14]

- Severe visual loss – bare or no light perception
- Intense ischemic retinal ischemia that extends beyond the macular area
- Little to no cherry-red spot
- Marked choroidal perfusion defects on fluorescein angiography
- Nonrecordable electroretinogram
- Late retinal pigment epithelium alterations

Ophthalmic artery obstruction is usually associated with local orbital or systemic diseases, which include orbital mucormycosis, orbital trauma, retrobulbar anesthesia, depot corticosteroid injection, atrial myxoma, or carotid artery disease. Temporal arteritis usually does not produce ophthalmic artery obstruction in the absence of ipsilateral ischemic optic neuropathy.

There is no proven therapy for ophthalmic artery obstruction, and visual prognosis is poor. Systemic workup is necessary to test for temporal arteritis, carotid artery disease, and cardiac disease.

6.1.8 Cilioretinal Artery Obstruction

A cilioretinal artery exists in about 30% of individuals. It is a vessel that perfuses the retina and is derived directly from the posterior ciliary circulation. As a result, this artery may remain patent in the case of central retinal artery obstruction. The cilioretinal arteries are usually observed to emanate from the temporal disc margin. They may be multiple and can also perfuse the nasal retina. Cilioretinal artery obstruction exists in three clinical variations:

- Isolated
- Cilioretinal artery obstruction combined with central retinal vein obstruction
- Cilioretinal artery obstruction combined with ischemic optic neuropathy

Isolated cilioretinal artery obstructions usually occur in young patients in collagen vascular disorders. These cases usually have good visual prognosis, with 90% of eyes improve to 20/40 (6/12) or better vision [15].

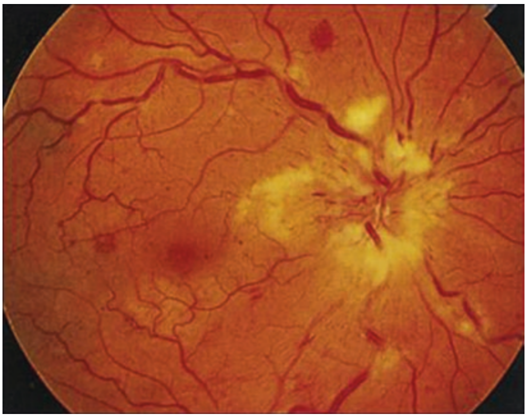


Fig. 6.3 Cilioretinal artery obstruction. In conjunction with mild nonischemic central retinal vein obstruction. Note the retinal ischemia inferior to the fovea in the distribution of the cilioretinal artery

Fig. 6.4 Combined central retinal artery obstruction and central retinal vein obstruction

Cilioretinal artery obstruction combined with central retinal vein obstruction is a fairly common variant in young patients (Fig. 6.3). It generally behaves as a nonischemic central retinal vein obstruction with a good central visual prognosis. One possible mechanism for this association is that some eyes develop a primary optic disc vasculitis (papillophlebitis) that affects both the arterial and venous circulations [16]. This disease is more common in men than in women and in healthy individuals. It has also been seen in conjunction with inflammatory bowel disease and leukemia.

In contrast to the first two groups discussed before, cilioretinal artery obstruction with ischemic optic neuropathy carries a poor visual prognosis and a strong association with temporal arteritis.

6.1.9 Combined Artery and Vein Obstructions

Central retinal artery obstruction combined with simultaneous central retinal vein obstruction is rare. These patients usually present with acute, severe loss of vision, usually to bare or no light perception. Examination shows a cherry-red spot combined with features of a central retinal vein obstruction, which include dilated, tortuous veins with retinal hemorrhages in all four quadrants (Fig. 6.4) [17]. Other systemic or local disease associations have been noted such as collagen vascular disorders, leukemia, orbital trauma, retrobulbar injections, and mucormycosis. The visual prognosis is poor, and the risk of neovascularization of the iris is about 75%. Spontaneous improvement had been noted in selected reports [18].

Branch retinal artery obstruction combined with simultaneous central retinal vein obstruction has also been reported [19]. This rare disease manifests as a central retinal vein obstruction. Neovascularization of the iris is possible, but systemic associations other than hypertension and diabetes have not been confirmed.

6.2 Branch Retinal Vein Obstruction

6.2.1 Introduction

Branch retinal vein obstruction (BRVO) is a common retinal vascular disorder of the elderly. Visual loss from a branch retinal vein occlusion usually is caused by macular edema, macular ischemia, or vitreous hemorrhage. In some patients, laser treatment can help stabilize or even improve vision.

6.2.2 Epidemiology and Pathogenesis

BRVOs occur approximately three times more commonly than CRVOs. Men and women are affected equally, with the usual age of onset between 60 and 70 years. Most epidemiological and histopathological evidence implicates arteriolar disease as the underlying pathogenesis. Branch retinal vein obstruction almost always occurs at an arteriovenous crossing, where the artery and vein share a common adventitial sheath. The artery nearly always is anterior (innermost) to the vein [20]. It is postulated that a rigid, arteriosclerotic artery compresses the retinal vein, which results in turbulent blood flow and endothelial damage, followed by thrombosis and obstruction of the vein. Most BRVOs occur superotemporally, probably because this is where the highest concentration of arteriovenous crossings lies.

Rarely, local ocular diseases, especially of an inflammatory nature, can result in a secondary BRVO. This has been reported in diseases such as toxoplasmosis, Eales' disease, Behçet's syndrome, and ocular sarcoidosis. Also, macroaneurysms, Coats' disease, retinal capillary hemangiomas, and optic disc drusen are linked to BRVO. Glaucoma is also a risk factor for the development of branch retinal vein occlusion. Branch retinal vein occlusion is usually unilateral, with only 9% of patients having bilateral involvement.

6.2.3 Ocular Manifestations

Patients with branch retinal vein occlusion usually complain of sudden onset of blurred vision or a visual field defect. Retinal hemorrhages confined to the distribution of a retinal vein are characteristic for BRVO (Fig. 6.5). As a result of the distribution, the hemorrhages usually assume a triangular configuration with the apex at the site of blockage. Flame-shaped hemorrhages predominate. Mild obstructions are associated with a relatively small amount of hemorrhage. Complete obstructions result in extensive intraretinal hemorrhages, cotton-wool spot formation, and widespread capillary nonperfusion. If the macular region is involved, macular edema, ischemia, or hemorrhage occur, which causes decreased visual acuity. Visual acuity may range from 20/20 (6/6) to counting fingers. If the macula is spared, a BRVO may be asymptomatic. Occasionally a partial BRVO with little hemorrhage and edema may progress to a completely occluded vein, with an increase in hemorrhage and edema and a corresponding decrease in visual acuity. Retinal neovascularization occurs in approximately 20% of cases. The incidence of retinal neovascularization rises with increasing area of retinal nonperfusion. Retinal neovascularization typically develops within the first 6–12 months but may occur years later. Vitreous hemorrhage can ensue and may require vitrectomy. Anterior segment neovascularization rarely is seen in patients with BRVO, unless other ischemic conditions coexist (e.g., diabetes). Severe cases may show a localized serous detachment of the macula or peripheral retina. Occasionally, a retinal break or detachment will occur from fibrovascular traction. With time, the dramatic picture of an acute BRVO can become much more subtle. Hemorrhages fade with time so that the fundus can look almost normal. Collateral vessels and microvascular abnormalities develop to help drain the affected area. The collateral vessels often cross the horizontal raphe. Proximal to the site of blockage, the retinal vein may become sclerotic. The retinal artery that feeds the affected zone may become narrowed and sheathed, as

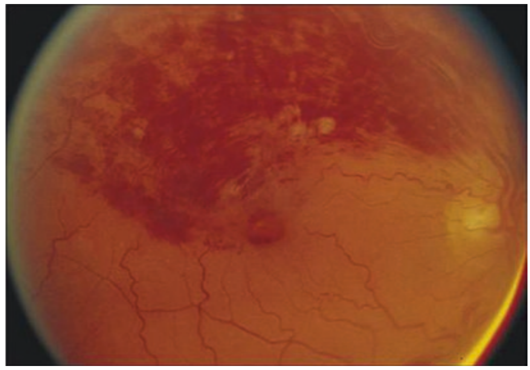


Fig. 6.5 Branch retinal vein obstruction. Fundus view of extensive retinal hemorrhages in segmental distribution of a superotemporal retinal vein. Dilated, tortuous veins, cotton-wool spots, and macular edema also can be seen

well. Microaneurysm formation occurs, and lipid exudation may be present. Capillary nonperfusion is seen best on fluorescein angiography in the later stages, after the hemorrhages have cleared. Epiretinal membrane and macular retinal pigment epithelial changes as a result of chronic cystoid macular edema sometimes are seen in the late phase of a BRVO. Retinal detachment, either rhegmatogenous or tractional, is uncommon but may be seen. Exudative localized retinal detachment in the distribution of the branch retinal vein occlusion also is seen if there is severe ischemia.

6.2.4 Diagnosis and Ancillary Testing

The diagnosis of an acute BRVO is made by finding retinal hemorrhages in the distribution of an obstructed retinal vein.

Fluorescein angiography is a helpful adjunct for both the establishment of the diagnosis and guidance for the treatment of BRVO. Arteriolar filling may be slowed in a severe BRVO, but venous filling in the affected vessel is almost always delayed in the acute phase. Hypofluorescence caused by hemorrhage and capillary nonperfusion are common findings, and dilated, tortuous capillaries are seen. Collateral vessels may cross the horizontal raphe. The retinal vessels, particularly the vein walls near the site of the occlusion, may stain with fluorescein. Neovascular fronds may leak fluorescein profusely. In contrast, collateral vessels do not leak fluorescein. Retinal vessels, particularly the vein walls, may stain with fluorescein, especially at the site of the occlusion. Macular edema, which is noted clinically but not angiographically, may indicate ischemia. Classic petaloid cystoid macular edema may involve the entire fovea or just several clock hours, depending on the distribution of the obstruction.

Optical coherence tomography testing can be helpful in patients with BRVO [21]. The newer generations of OCT are so sensitive that CME can sometimes be detected when it is not visible on clinical exam or on fluorescein angiography. OCT testing also shows serous macular detachments in more than two thirds of patients, and this is not always apparent on clinical exam alone. Retinal hemorrhages and lipid exudates, as well as ERMs, are also common findings on OCT testing in BRVO.

6.2.5 Differential Diagnosis

The differential diagnosis of BRVOs is shown in Table 6.2.

6.2.6 Systemic Associations

Hypertension is the condition most commonly associated with BRVO. The Eye Disease Case-Control Study clearly demonstrated the important association of hypertension with vein obstructions [22]. In that study, more than 50% of BRVOs were associated with hypertension. The study also found an association between vein obstructions and a history of cardiovascular disease, increased body mass index at 20 years of age, glaucoma, and higher serum levels of α_2-globulin. A reduced risk of BRVO was found with alcohol consumption and increasing levels of high-density lipoprotein cholesterol levels.

6.2.7 Pathology

A histopathological study of nine branch vein occlusions showed a fresh or recanalized thrombus at the site of the vein occlusion in all eyes [23]. Ischemic atrophy of the retina was found in the distribution of the occlusion in most of the eyes. All eyes showed varied degrees of arterio-

Table 6.2 Differential diagnosis of branch retinal vein obstruction

Hypertensive retinopathy
Diabetic retinopathy
Ocular ischemic syndrome
Juxtafoveal retinal telangiectasia
Combined branch retinal artery and branch retinal vein occlusion
Radiation retinopathy

sclerosis. No thrombus was noted in any of the arteries. Neovascularization of the disc and retina was noted in four eyes, and cystoid macular edema was present in five.

6.2.8 Treatment

The Branch Vein Occlusion Study represented a major advance in the understanding of the treatments for two of the most significant complications of branch vein occlusions, namely, macular edema and neovascularization [24, 25]. The study found that a grid pattern laser treatment helped to reduce macular edema and improved visual acuity. In patients who have 20/40 (6/12) or worse vision and macular edema on fluorescein angiography, laser treatment improved the chances of a two or more line improvement in vision on the Snellen chart when compared with untreated controls [24, 25] (65% versus 37%). Because visual acuity and macular edema may improve spontaneously, patients were not treated with laser for at least 3 months after the development of the vein obstruction, to allow for spontaneous improvement. Also, treatment was delayed if the intraretinal hemorrhage was too dense to allow either photocoagulation or adequate evaluation with fluorescein angiography. Patients who had hemorrhage directly in the fovea were excluded. A fluorescein angiogram less than 1 month old was used to guide treatment. A grid pattern of laser was applied to the area of capillary leakage (Fig. 6.6).

Photocoagulation did not extend closer than the edge of the foveal avascular zone, nor did it extend peripherally beyond the major vascular arcades. The eyes were reevaluated with fluorescein angiography 4 months after treatment, and additional photocoagulation was applied if the vision remained poor and macular edema persisted. Many patients require only one treatment, but multiple treatments may be necessary and are often effective [26]. Typically, a 50–100 μm spot size is used, and medium-white burns, each of 0.1 s duration, are applied to the area of edema. In both treated and controlled groups, patients who had hypertension tended to respond less favorably to laser treatment.

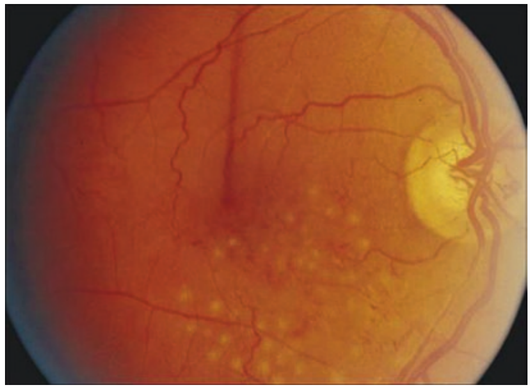


Fig. 6.6 Branch retinal vein obstruction. Immediate post-treatment view of grid laser treatment for macular edema secondary to a BRVO

Table 6.3 Treatment guidelines for branch retinal vein occlusion and macular edema

For macular edema, visual acuity of 20/40 (6/12) or worse
Wait for clearance of retinal hemorrhage to allow adequate fluorescein angiography
Determine if decreased visual acuity is caused by macular edema (versus macular nonperfusion)
If macular edema explains visual loss, and no spontaneous improvement has occurred by 3 months, grid macular photocoagulation is recommended
If capillary nonperfusion explains decreased visual acuity, laser treatment is not advised

The Branch Vein Occlusion Study Group also evaluated the efficacy and timing of sectorial PRP for retinal neovascularization and vitreous hemorrhage [24]. In patients with neovascularization treated with laser, only 29% developed vitreous hemorrhage versus 61% of those untreated. The data showed no advantage with treatment before neovascularization occurred, even if extensive capillary nonperfusion existed. If laser is applied to all nonperfused BRVOs, a large percentage of patients will be treated unnecessarily (Tables 6.3 and 6.4). Fluorescein angiography can be helpful in guiding laser treatment, because it will help define areas of capillary nonperfusion. A scatter pattern of laser is performed in the affected sector. Typically, 500 μm-sized medium-white burns are applied, extending from the arcade out to the periphery. Fill-in PRP may be applied if neovascularization progresses or if

Table 6.4 Treatment guidelines for branch retinal vein occlusion and neovascularization

Good-quality fluorescein angiography is obtained after retinal hemorrhages have cleared sufficiently
If more than five disc diameters of nonperfusion are present, the patient should be followed at 4-month intervals to seek the development of neovascularization
If neovascularization develops, panretinal photocoagulation to the involved retinal sector should be applied using argon laser to achieve "medium"-white burns, 200–500 mm in diameter – one burn width apart to cover the entire involved segment

vitreous hemorrhage occurs. Vitreous surgery is employed occasionally for nonclearing vitreous hemorrhages, epiretinal membrane, or tractional retinal detachment with macular involvement. The outcomes are generally favorable, although preexisting pathology frequently limits recovery of good vision [27].

6.2.9 Course and Outcome

Without treatment, one third of patients who have branch retinal vein occlusion end up with visual acuity better than 20/40 (6/12). However, two thirds have decreased visual acuity secondary to macular edema, macular ischemia, macular hemorrhage, or vitreous hemorrhage. As noted above, laser treatment for macular edema significantly enhances the chance that the patient's baseline visual acuity will improve by two lines (65% versus 37%). The mean number of lines of improvement in visual acuity averages 1.33 in treated patients versus 0.23 in the control group. Poor visual prognostic factors include advancing age, male sex, worse baseline visual acuity, and an increased number of risk factors [28]. Good prognosis is associated with a younger age, female sex, and fewer risk factors. Patients should be followed up every 3–4 months.

Approximately 20% of patients with branch retinal vein occlusion will develop neovascularization. Of these patients, about 60% will have episodic vitreous hemorrhages. Fortunately, laser treatment (sector PRP) can reduce this by one half to 30%.

6.2.10 New Treatments for Branch Retinal Vein Occlusion

There is a growing interest in pharmacologic and surgical therapies for BRVO. The use of intravitreal triamcinolone to treat macular edema due to BRVO is becoming increasingly popular [29, 30]. A number of studies report improvement of visual acuity and reduction in macular edema following intravitreal injections of between 4 and 20 mg of triamcinolone acetonide (Figs. 6.7 and 6.8). Enthusiasm for this treatment modality has been tempered by the limited duration of the treatment effect (2–9 months), the frequent need for re-treatments, a 40% rate of steroid-related pressure rise, a 1–2% chance of pressure spike severe enough to require glaucoma filtration surgery, and, in phakic patients, a 25% chance of cataract surgery within a year of the treatment. Drugs that inhibit VEGF such as bevacizumab (e.g., Avastin) are being evaluated in the treatment of both macular edema and neovascularization associated with BRVO [31, 32]. As a result of the recent introduction of these drugs, there is a great interest in determining how to best utilize these medications.

Surgical treatments for BRVO have been described including vitrectomy, ILM peeling, sheathotomy, and venous cannulation [33–36]. The reports on these modalities are exciting and represent the continued evolution of the treatment of BRVO.

6.3 Inflammatory Optic Neuropathies and Neuroretinitis

6.3.1 Introduction

Inflammatory optic neuropathy, or optic neuritis, is referred to as *papillitis* when the optic disc is swollen and *retrobulbar optic neuritis* when the disc appears normal. The most common form of optic neuritis is acute demyelinating optic neuritis. We have derived much of our knowledge about this disease entity from the Optic Neuritis Treatment Trial (ONTT). This multicenter study

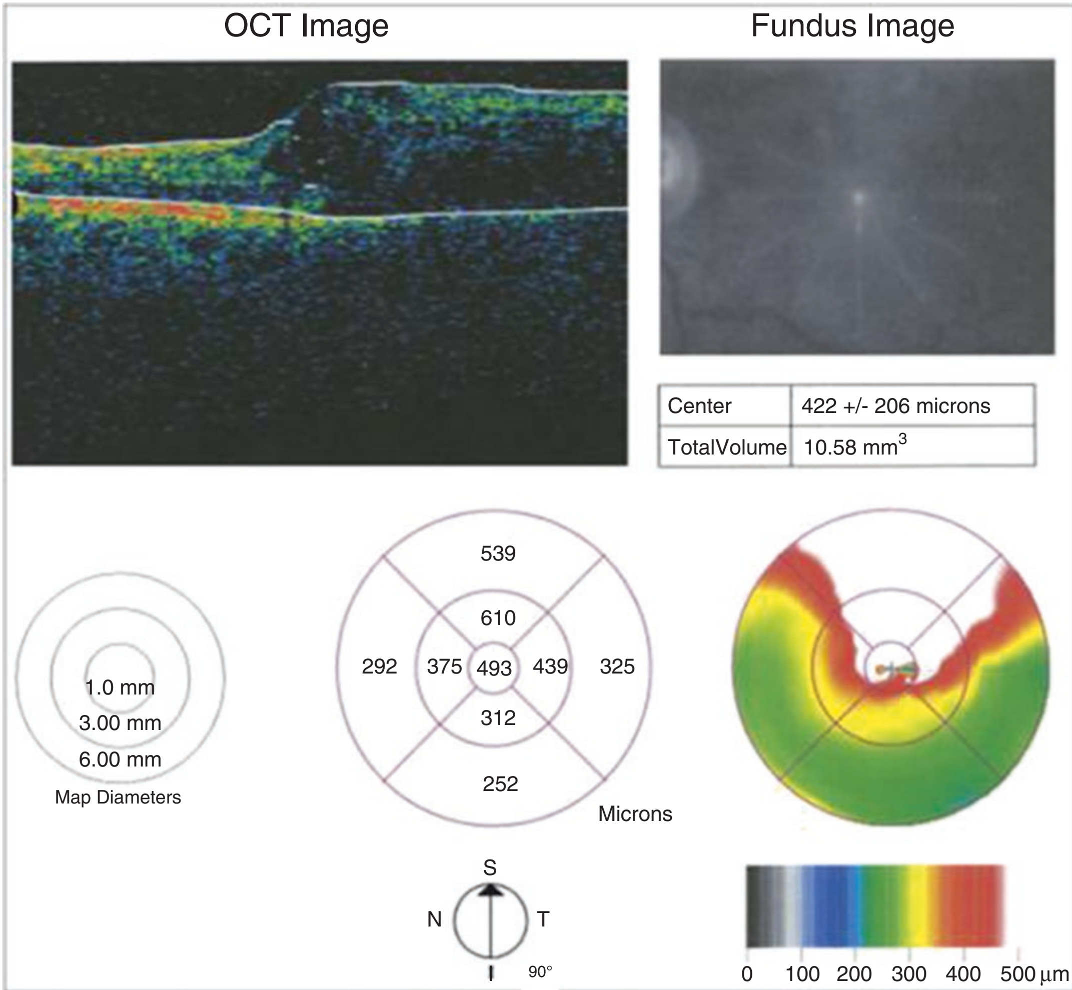


Fig. 6.7 Optical coherence tomography of a patient with a superotemporal branch retinal vein occlusion. There are marked macular edema and subretinal fluid present

trial assessed the benefit of corticosteroid treatment of optic neuritis and studied the relationship between optic neuritis and multiple sclerosis (MS) [37–52].

6.3.1.1 Epidemiology and Pathogenesis

The annual incidence of optic neuritis is approximately 3–5 per 100,000 per year [53], while the prevalence is 115 per 100,000 [54]. Women are affected more commonly than men, with most patients age between 20 and 50 years. In most cases, the pathogenesis of optic neuritis is inflammatory demyelination, whether or not MS is diagnosed clinically [55, 56]. It is likely that many cases of monosymptomatic optic neuritis occur as the initial manifestation of MS [57].

6.3.2 Ocular Manifestations

Patients with acute demyelinating optic neuritis usually present with abrupt loss of vision which occurs over several hours to days. Progression for more than 1 week or failure of recovery to begin within 4 weeks would suggest an alternative

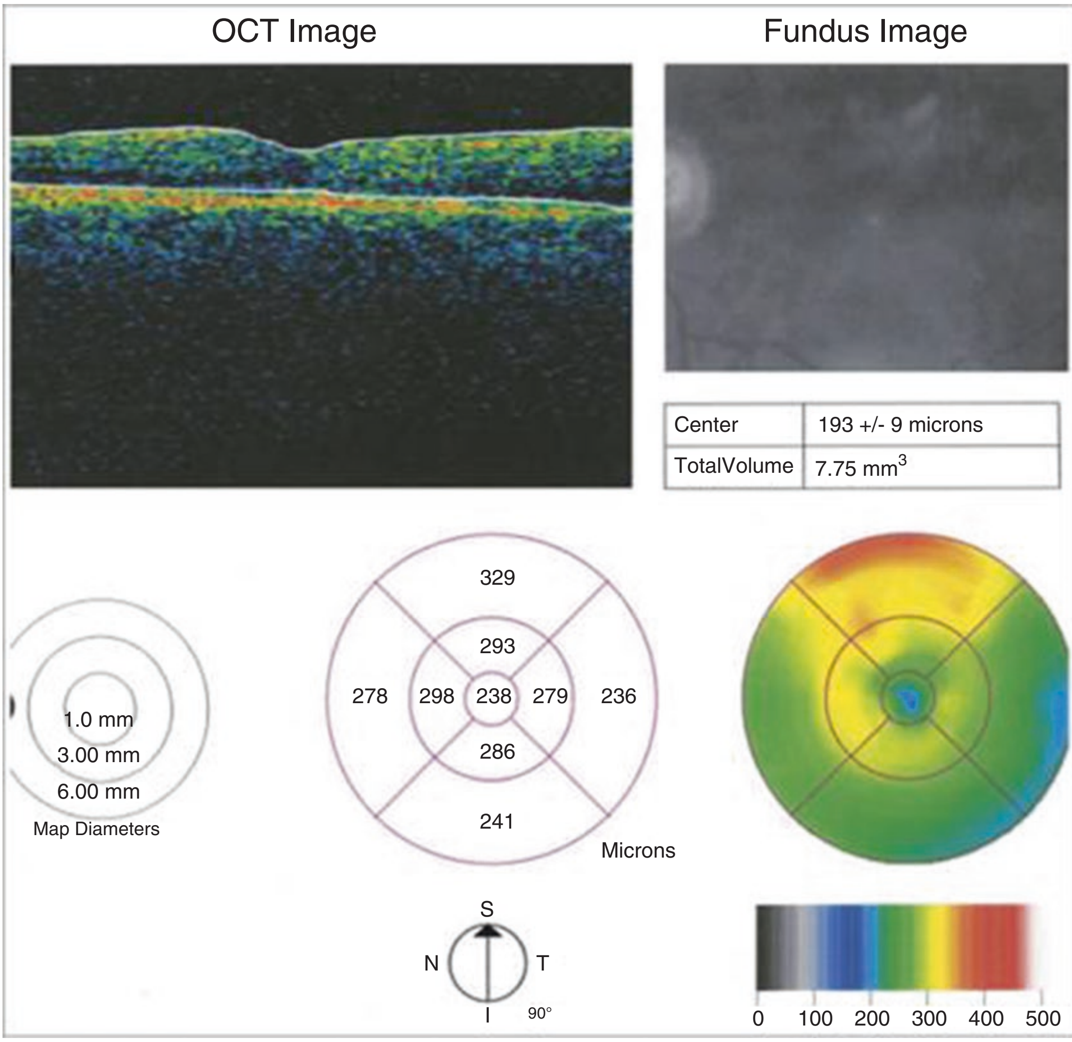


Fig. 6.8 Optical coherence tomography of the patient after 4 mg of intravitreal triamcinolone

underlying cause [58–63]. Visual loss is usually monocular, although occasionally both eyes are affected simultaneously, particularly in children.

Mild pain in or around the eye, especially with eye movement, is present in more than 90% of patients and generally lasts no more than a few days. The presence of pain on eye movement is a helpful (although not definitive) clinical feature that differentiates acute demyelinating optic neuritis from nonarteritic anterior ischemic optic neuropathy (AION) [64].

On examination, optic nerve dysfunction is evident. The degree of vision loss can vary from a mild visual field defect to severe loss of central acuity (3% of ONTT participants had no light perception, and 90% described at least some loss of central acuity) [39]. Severe loss of visual acuity is more common in children [65]. Color vision and contrast sensitivity are impaired in almost all cases, often out of proportion to visual acuity. Visual field loss, which may be diffuse (48%) or focal (i.e., nerve fiber bundle defects, central or cecocentral scotomas, hemianopic defects), is also common in acute optic neuritis [40]. Altitudinal defects (focal visual field loss above or below the horizontal meridian) are less common and should prompt consideration of a diagnosis of anterior ischemic optic neuropathy (AION) [65].

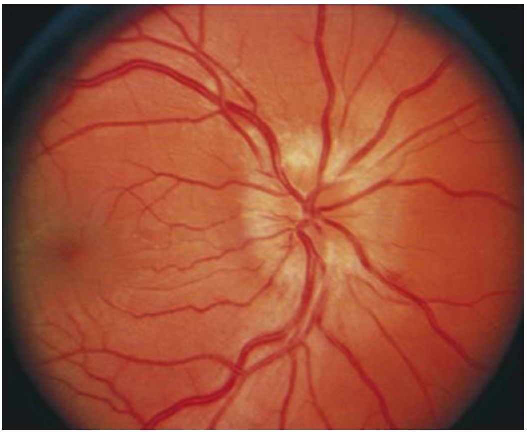


Fig. 6.9 Optic disc swelling (papillitis) associated with acute optic neuritis

Low-contrast letter acuity has recently emerged as a very sensitive test for optic neuropathy [66]. An afferent pupillary defect (APD) is detected in almost all unilateral cases of optic neuritis. If an APD is not present, a preexisting optic neuropathy in the fellow eye must be suspected. Asymptomatic visual dysfunction is reported to be common among fellow eyes of patients who have apparent unilateral optic neuritis [43].

The optic disc appears normal in approximately two thirds of adults with acute demyelinating optic neuritis (retrobulbar optic neuritis), while disc swelling is present in about one third of adult cases (papillitis) (Fig. 6.9); children with optic neuritis experience optic disc swelling more frequently than adults do [65]. Funduscopic features of optic disc swelling include elevation of the optic nerve head, disc hyperemia, blurring of the disc margins, and edema of the nerve fiber layer [67]. Although the clinical features are similar in both forms, optic disc hemorrhages were uncommon in the ONTT (6%), and their presence should suggest an alternative diagnosis.

6.3.3 Diagnosis and Ancillary Testing

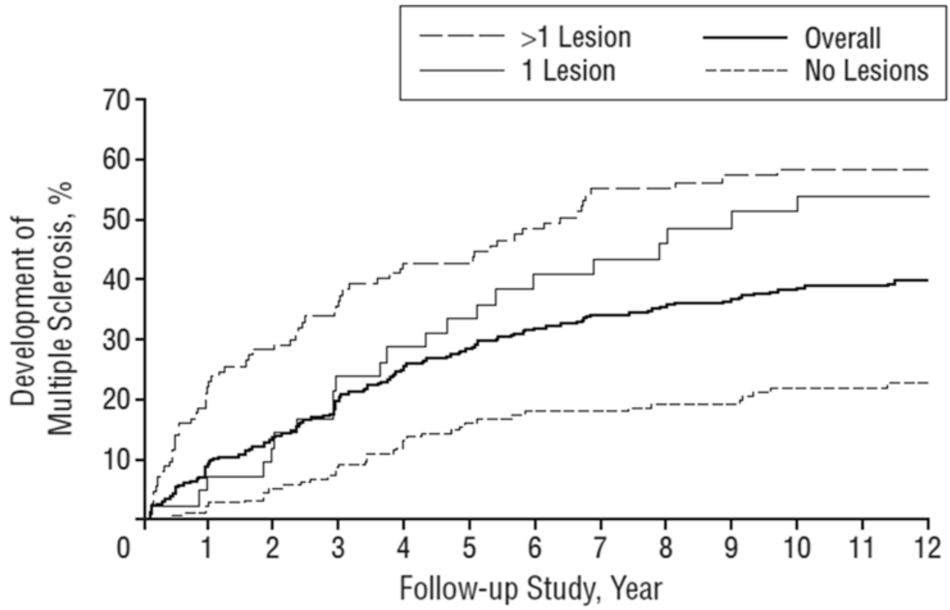
The diagnosis of acute optic neuritis is based on an appropriate medical history (typical versus atypical course) and clinical signs and symptoms as described above. Diagnostic tests, including magnetic resonance imaging (MRI), cerebrospinal fluid (CSF) analysis, and serological studies, usually are performed to rule out noninflammatory etiologies such as a compressive lesion [46, 47, 52].

MRI of the brain and orbits with fat suppression and gadolinium should be performed to confirm the diagnosis of optic neuritis and to assess for the presence of other white matter lesions (Fig. 6.10) [46, 47, 52]. Optical coherence tomography (OCT) may be useful in predicting the subset of optic neuritis patients who will suffer persistent visual dysfunction; a 2006 study of 54 patients documented a poor visual outcome in patients with a retinal nerve fiber layer (RNFL) thickness of less than 75 μm measured with OCT within 3–6 months of an initial optic neuritis event [68].

6.3.4 Differential Diagnosis

The differential diagnosis for acute optic neuropathy is outlined in Table 6.5. When there are acute visual loss and unilateral optic disc swelling, both optic neuritis and AION must be considered. AION is typically painless, occurs in older patients over 50 years of age, and may be associated with optic disc hemorrhages. When the optic disc is normal in patients with unilateral optic neuropathy, a compressive lesion must be excluded, in which case a progressive visual loss persists beyond the typical period of 1–2 weeks.

Fig. 6.10 (continued) number of patients classified as having multiple sclerosis during each yearly interval. The "censored" rows indicate the number of patients not developing multiple sclerosis whose last available follow-up data occurred during each yearly interval. Asterisk indicates 37 patients who had no baseline MRIs (From Optic Neuritis Study Group. High- and low-risk profiles for the development of multiple sclerosis within 10 years after optic neuritis: experience of the Optic Neuritis Treatment Trial. Arch Ophthalmol. 2003;121:944–9.)



Overall												
Patients at Risk	388*	340	317	290	271	253	232	218	210	207	199	162
Multiple Sclerosis	33	17	23	18	13	12	8	4	3	6	2	2
Censored	15	6	4	1	5	9	6	4	0	2	35	79
Brain MRI: No Lesion												
Patients at Risk	191	177	168	159	152	142	133	129	126	126	121	97
Multiple Sclerosis	4	5	6	6	7	3	0	2	0	4	0	1
Censored	10	4	3	1	3	6	4	1	0	1	24	54
Brain MRI: 1 Lesion												
Patients at Risk	44	39	37	32	30	27	23	22	21	20	19	16
Multiple Sclerosis	3	2	5	2	2	3	1	1	1	1	1	0
Censored	2	0	0	0	1	1	0	0	0	0	2	8
Brain MRI: >1 Lesion												
Patients at Risk	116	90	80	71	64	62	55	46	44	42	40	32
Multiple Sclerosis	24	8	8	7	1	6	7	0	2	1	0	0
Censored	2	2	1	0	1	1	2	2	0	1	8	9

Fig. 6.10 The development of multiple sclerosis was strongly associated with the presence of one or more lesions on the baseline MRI of the brain in a 10-year follow-up of the Optic Neuritis Treatment Trial (ONTT) [68]. The cumulative probability of multiple sclerosis was statistically significantly higher in patients with one or more lesions seen on the baseline magnetic resonance imaging (MRI) scan of the brain than in patients with no brain lesions ($P < 0.001$, log rank test) but was not significantly different comparing patients with a single brain lesion and patients with multiple lesions ($P = 0.22$, log rank test). The numbers of patients at risk are the numbers who had not developed multiple sclerosis at the beginning of each year. The "multiple sclerosis" rows indicate the

Table 6.5 Differential diagnosis of acute unilateral optic neuropathy

Anterior ischemic optic neuropathy
Tumor
Aneurysm
Vasculitis
Neuroretinitis
Metastatic carcinoma
Lymphoreticular disorder
Sinusitis
Granulomatous inflammation
Leber's hereditary optic neuropathy

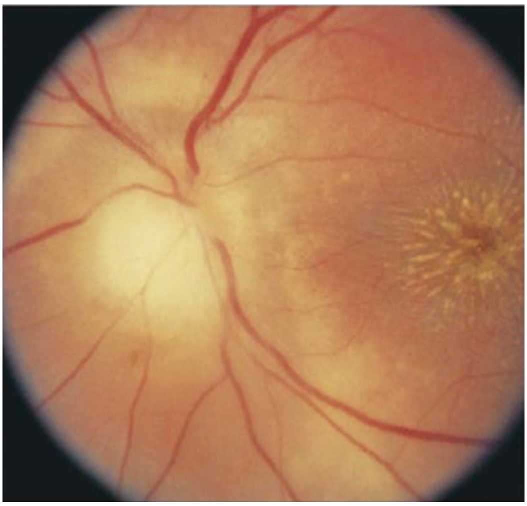


Fig. 6.11 Neuroretinitis with optic disc edema and macular star formation

Other inflammatory, infectious, and neoplastic disorders may produce infiltration or demyelination, or both, of the optic nerve. These conditions may appear as either acute or progressive visual loss (sarcoidosis, systemic lupus erythematosus, syphilis, postviral syndromes, lymphoma, and leukemia). The treatment of optic neuritis in these systemic disorders is dictated by guidelines for appropriate treatment of the underlying diseases [67].

Neuroretinitis with optic disc edema and macular exudates must be differentiated from acute demyelinating optic neuritis (Fig. 6.11). Most cases of neuroretinitis are idiopathic, but the diagnosis requires the exclusion of infectious causes such as *Bartonella henselae* (cat-scratch disease), *Toxoplasma gondii* (toxoplasmosis), *Treponema pallidum* (syphilis), *Toxocara canis* (toxocariasis), *Borrelia burgdorferi* (Lyme disease), *Leptospira* spp. (leptospirosis), *Mycobacterium tuberculosis* (tuberculosis), *Histoplasma capsulatum* (histoplasmosis), *Rickettsia typhi* (murine typhus), and *Brucella* spp. (brucellosis); nonspecific viral syndromes and viral etiologies involving Epstein-Barr virus (EBV), herpes simplex virus (HSV), human immunodeficiency virus (HIV), mumps, or hepatitis B or C have also been implicated [69]. Absence of these typical features should suggest other causes of inflammatory optic neuropathy or alternative diagnoses (e.g., sarcoidosis, systemic lupus and other vasculitides, paraneoplastic disease, syphilis, Lyme disease, *Bartonella henselae* infection (associated with cat-scratch neuroretinitis), ischemic optic neuropathy, or Leber's hereditary optic neuropathy) [51, 58–63].

The time course of symptom onset distinguishes demyelinating optic neuritis from other inflammatory or compressive optic neuropathies in which visual function may worsen relentlessly over a period of weeks to months (e.g., sarcoid neuropathy, meningioma, or pituitary adenoma).

Optic neuritis is more frequently bilateral in children than in adults and is more commonly associated with optic disc swelling in children than in adults.

These ophthalmoscopic findings were associated with an extremely low risk or no risk of multiple sclerosis within 10 years of follow-up among patients in the Optic Neuritis Treatment Trial.

Data are from the Ischemic Optic Neuropathy Decompression Trial.

6.3.4.1 Viral and Postviral Syndromes

These cases of optic neuritis typically follow the onset of a viral infection by 1–3 weeks, but it also can occur as a postvaccination phenomenon. It is more common in children and likely occurs by an immunological process that produces optic nerve demyelination. Postviral optic neuritis may be unilateral but is frequently bilateral. The optic discs may appear normal or swollen; retinal involvement (neuroretinitis) is common when there is

optic disc swelling. Associated meningoencephalitis can occur. Visual prognosis after parainfectious optic neuritis is excellent, even with no treatment. Corticosteroid treatment can be considered in cases of bilateral, severe visual loss.

6.3.4.2 Sarcoidosis

Granulomatous inflammation of the optic nerve is a frequent ocular manifestation of sarcoidosis. Clinical findings may be similar to those of acute demyelinating optic neuritis. The optic disc may have a characteristic lumpy, white appearance, suggestive of granulomatous infiltration. Visual recovery is rapid in most cases following corticosteroid treatment. Neuroretinitis is an uncommon in sarcoidosis [70].

6.3.4.3 Syphilis

Syphilitic optic neuritis has become more common with the increased prevalence of human HIV infection. Optic nerve involvement may be unilateral or bilateral. Vitritis is a typical feature that differentiates syphilis infection from acute demyelinating optic neuritis, in which the vitreous is typically clear. The diagnosis is established with positive syphilis serological and CSF VDRL (Venereal Disease Research Laboratories) test results. Treatment with aqueous crystalline penicillin G, 18–24 million units per day, administered as 3–4million units i.v. every 4 h (or continuous infusion) for 14 days produces visual recovery in most cases; however, recurrences are possible [71]. Secondary syphilis can also manifest as neuroretinitis, with variable severity of visual loss.

6.3.4.4 Lyme Disease

Although optic neuritis has been reported in patients with positive Lyme serological test (ELISA and Western blot) results or other neurological findings suggestive of Lyme disease, definitive evidence of a causal relationship with *B. burgdorferi* infection has not been established in most cases [72, 73]. However, patients with neurological or ocular manifestations should, in most cases, receive a 2–4-week course of i.v. ceftriaxone or alternative agent, with resolution of related symptoms within weeks [73, 74]. Syphilis infection may produce false-positive Lyme disease serological examination results and, therefore, must also be considered in patients with optic neuropathy or other neurological manifestations.

6.3.4.5 Cat-Scratch Disease (CSD)

Bartonella henselae is implicated in numerous ophthalmic disease states, including neuroretinitis. The prevalence of neuroretinitis in CSD is documented to be between 1% and 2%; however, as was shown in a 2000 retrospective study, among patients who develop neuroretinitis, nearly two thirds show serologic evidence of past or present CSD infection (9/14 tested patients, or 64%) suggesting that CSD may be the most common cause of neuroretinitis [75]. Patients with CSD ophthalmopathy show classic ophthalmoscopic signs of neuroretinitis, including diffuse disc edema, nerve fiber layer hemorrhages, cotton-wool spots, multiple discrete lesions in the deep retina, and stellate macular exudates. Such patients have diminished visual acuities ranging from 20/25 to counting fingers; APDs, dyschromatopsia, and visual field abnormalities are common. CSD neuroretinitis may be unilateral or bilateral, as well as asymptomatic, and generally has a benign course with an excellent prognosis for visual recovery to 20/40 or better. A small subset of patients may experience a prolonged febrile illness and remain more severely impaired, with failure to regain baseline visual acuity.

Early therapy with oral doxycycline (for patients older than 8 years) or erythromycin (for younger patients) and rifampin for 4–6 weeks promotes resolution of CSD neuroretinitis and truncates the systemic infection, typically resulting in regression of posterior pole findings and the return of 20/20 visual acuity after 1–4 weeks of therapy. Long-term use of doxycycline or a macrolide may also be useful for preventing recurrences in HIV-positive patients [76, 77].

6.3.4.6 Toxoplasmosis

Optic neuropathies are common in patients with *Toxoplasma gondii* infection, the most important protozoan cause of intraocular inflammation in the world, and include retinochoroiditis, papilli-

tis, and neuroretinitis [78, 79]. Ocular lesions primarily affect the retina, and the hallmark of the disease is focal necrotizing retinitis, ultimately resulting in characteristic atrophic scars. Active retinal lesions are oval or circular, with a cream-colored retina and surrounding retinal thickening due to necrosis and edema. Common symptoms include black floating spots, blurred vision, ocular pain, and redness and, if the visual axis or macula is involved, severely reduced vision. The disease is bilateral in 40% of cases, almost exclusively in the immunocompromised. It is usually a self-limiting disease in non-AIDS patients, and, without treatment, inflammation gradually subsides, and the lesions heal in 6–8 weeks.

6.3.4.7 Optic Neuritis in HIV Disease

Many infectious diseases in HIV patient may cause optic neuropathy, including tuberculosis, toxoplasmosis, toxocariasis, cytomegalovirus, herpes zoster, *Cryptococcus*, and other fungi. Primary central nervous system lymphoma infiltrating the optic nerves and chiasm has been reported recently in patients with HIV [80].

6.3.4.8 Systemic Lupus Erythematosus and Other Vasculitides

Optic neuritis may occur in patients with systemic lupus erythematosus (SLE), polyarteritis nodosa, and other systemic vasculitides. About 1% of SLE may have optic nerve involvement. It is likely due to ischemia, which may produce demyelination alone or in combination with axonal necrosis. Clinical manifestations may include those of acute optic neuritis (both papillitis and retrobulbar neuritis), acute ischemic optic neuropathy, or chronic progressive visual loss. Treatment with high-dose corticosteroids is indicated and has been reported to reverse severe visual loss [81].

6.3.5 Systemic Associations

Acute demyelinating optic neuritis occurs most often in MS (among 50% of patients with MS) and frequently represents the first clinical manifestation of MS (in 20% of patients with MS) [45, 46, 57, 82]. A follow-up of the ONTT cohort to 10 years has continued to demonstrate that brain MRI is the most powerful predictor of subsequent MS risk in monosymptomatic patients [45, 46, 52]. The presence of one or more white matter lesions was associated with a 56% risk of MS after 10 years, while the risk was only 22% if the MRI results were normal (excluding optic nerve enhancement) [45, 52]. The risk with multiple lesions was not significantly higher than it was with a single lesion (58% versus 51%; $P = 0.22$, log rank test) [52]. Monosymptomatic patients with one or more brain white matter lesions seen with MRI are, therefore, considered to be at high risk for the development of MS following acute demyelinating optic neuritis. Among patients with normal brain MRI findings (no white matter lesions) in the ONTT, the presence of optic disc swelling, mild visual acuity loss, and male gender were features associated with a reduced risk of MS [46, 52]. Painless visual loss, total visual loss (no light perception), and ophthalmoscopic findings of severe disc swelling, hemorrhage of the optic disc or surrounding retina, or retinal exudates were features associated with a 0% risk of MS in these patients [52]. In patients with a normal baseline brain, certain features (severe optic disc swelling, hemorrhages, and exudates) suggest a low risk of developing MS [52].

As in adults, optic neuritis is predictive of the subsequent risk of MS in children; one longitudinal study found that MS developed in 13% of children within 10 years of the first episode of optic neuritis and in 19% within 20 years of the first episode [83].

6.3.6 Pathology

The pathophysiology of acute optic neuritis and MS is that of primary inflammatory demyelination [55, 56]. The inflammatory response in MS plaques is marked by perivascular cuffing, T cells, and plasma cells. Although a disease of myelin with sparing of nerve axons, neuronal and axonal loss have been demonstrated to occur in MS patients [55].

6.3.7 Treatment

According to ONTT, intravenous methylprednisolone treatment hastens recovery of visual function but does not affect long-term visual outcome; this benefit was greatest in the first 15 days. Oral prednisone alone (without intravenous methylprednisolone) unexpectedly showed an increased risk of recurrent optic neuritis (30% after 2 years versus 16% for the placebo group and 13% for those receiving intravenous steroids) that has persisted throughout the 10-year follow-up period (44% after 10 years versus 31% for the placebo group and 29% for those receiving intravenous steroids) [44, 46, 51]. Monosymptomatic patients in the intravenous methylprednisolone group had a reduced rate of development of MS during the first 2 years of follow-up, but this benefit did not persist beyond 2 years and was seen only in patients with brain MRI scans that indicated a high risk for subsequent MS (originally described as MRI scans with two or more white matter lesions; 10-year follow-up data has confirmed one or more white matter lesions as an equivalent risk) [45, 46, 52].

The Controlled High-Risk Avonex MS Prevention Study (CHAMPS) demonstrated that treatment with interferon β-1a (Avonex) following acute monosymptomatic demyelinating optic neuritis or other first demyelinating event (including brainstem syndrome or incomplete transverse myelopathy) significantly reduces the 3-year cumulative probability of MS [82]. Participants in the interferon β-1a group also had significantly reduced rates of accumulation of new but clinically silent lesions on brain MRI (P <0.001 for both T2-enhancing and gadolinium-enhancing lesions after 18 months of follow-up). Results were similar in the subgroup of patients who experienced optic neuritis as their first demyelinating event (192 patients), supporting the initiation of interferon β-1a in patients at high risk for MS by MRI criteria [84]. All patients (interferon β-1a and placebo groups) also received a 3-day course of intravenous methylprednisolone followed by oral prednisone, as per the ONTT protocol.

An extension study (Controlled High-Risk Avonex Multiple Sclerosis Prevention Study in Ongoing Neurological Surveillance, known as CHAMPIONS) provided the rationale for early therapy and confirmed the potential for long-term benefit of interferon β-1a in patients with acute monosymptomatic demyelinating optic neuritis (or other first demyelinating event) and high-risk brain MRI findings [41]. Early interferon therapy following a first demyelinating event is likewise supported by results of a randomized trial of interferon β-1a (Rebif) performed in Europe (Early Treatment of Multiple Sclerosis Study, ETOMS) [85].

Results from the Betaferon/Betaseron in Newly Emerging Multiple Sclerosis for Initial Treatment (BENEFIT) trial, involving 487 patients with a first clinical demyelinating event (80 patients with optic neuritis), suggest that 250 μg of interferon β-1b (Betaseron) subcutaneously every other day delays the development of multiple sclerosis [86]. Consistent with other studies, multiple sclerosis was significantly less likely to be diagnosed in the interferon group within 2 years of follow-up compared with the placebo group (28% versus 45%). Patients in the interferon group also had significantly fewer lesions on brain MRI than did patients in the placebo group.

6.3.7.1 Other Treatments

In experimental models of MS, intravenous immunoglobulin G (IVIG) has been shown to promote remyelination of the central nervous system [87]. A 1992 study suggested that IVIG treatment may have some benefit in patients with resolved optic neuritis who have significant visual deficits [88]. However, two recent randomized trials of IVIG versus placebo have failed to demonstrate any clinical benefit [89, 90].

6.3.7.2 Management Recommendations

In patients with a typical clinical course and examination findings for acute monosymptomatic demyelinating optic neuritis (first demyelinating event), MRI of the brain (T2-enhanced and

gadolinium-enhanced images) should be performed to determine whether they are at high risk for the development of MS. Characteristic demyelinating lesions in patients at risk for multiple sclerosis are 3 mm or larger in diameter, are ovoid, are located in periventricular areas of the white matter, and radiate toward the ventricular spaces [82, 84–86]. Oligoclonal banding of proteins in the cerebrospinal fluid is a useful predictor of the risk of multiple sclerosis among patients with either normal brain MRI or abnormal findings that are not classic for demyelination (e.g., small, punctate lesions that are not periventricular or ovoid) [91]. In the case of two or more white matter lesions on MRI (3 mm diameter or larger, at least one lesion periventricular or ovoid), the following treatment options should be considered: [37–52, 82, 84–86, 92]

- Intravenous methylprednisolone (1 g per day, single or divided doses, for 3 days) followed by oral prednisone (1 mg/kg per day for 11 days, then 4-day taper)
- Interferon β-1a (Avonex 30 μg intramuscularly once a week)
- Interferon β-1a (Rebif 22 μg subcutaneously once a week)
- Betaseron (250 μg subcutaneously every other day)

In monosymptomatic patients who have fewer than two MRI white matter lesions and in those for whom a diagnosis of MS has been established, intravenous methylprednisolone treatment (followed by oral prednisone as outlined) may be considered on an individual basis to hasten visual recovery, but this has not been demonstrated to improve long-term visual outcome. The effects of corticosteroid treatment and other therapies on the recovery of visual function and on the risk of multiple sclerosis in children have not been established by randomized trials, but intravenous methylprednisolone treatment is generally recommended if visual loss is unilateral and severe or is bilateral [93].

Based on findings from the ONTT, oral prednisone alone (without prior treatment with intravenous methylprednisolone) may increase the risk of recurrent optic neuritis and should be avoided.

A short course of nonsteroidal anti-inflammatory agents may be helpful in the occasional case of disabling pain associated with optic neuritis [67].

6.3.8 Course and Outcome

Most patients start to recover vision within 2–3 weeks of symptom onset even without treatment. Visual improvement usually begins rapidly in patients treated with intravenous methylprednisolone. Once recovery begins, most patients achieve near maximal improvement within 1–2 months, although recovery up to 1 year is possible. Severity of the initial visual loss appears to be the only predictor of visual outcome [38, 51].

Despite favorable recovery of vision, frequently to 20/20 or better (as was seen in 74% of patients in 10-year ONTT follow-up) [51], many patients with acute demyelinating optic neuritis continue to experience subtle visual abnormalities that affect their daily function and quality of life; they may report that their vision seems blurred, washed out, or "not right." [48, 49] Persistent abnormalities of visual acuity (15–30%), contrast sensitivity (63–100%), color vision (33–100%), the visual field (62–100%), stereopsis (89%), light brightness sense (89–100%), afferent pupillary reaction (55–92%), optic disc appearance (60–80%), and the visual-evoked potential (63–100%) have been demonstrated in such patients. Recurrent episodes of optic neuritis in the initially affected or fellow eye may occur also; approximately 35% of placebo-group ONTT participants had a second episode in either eye within the 10-year follow-up period, and risk of recurrence is twofold greater in patients with an MS diagnosis at any time during 10-year follow-up than in patients who do not develop MS (48% versus 24%; P <0.001) [45, 51].

During and even beyond the recovery of vision following acute demyelinating optic neuritis, patients frequently experience transient worsening of symptoms with exposure to heat (Uhthoff's

symptom) [94]. Positive visual phenomena and photopsias are also common and were reported by 30% of ONTT participants [37, 39].

6.4 Ischemic Optic Neuropathies

6.4.1 Introduction

Optic nerve ischemia most frequently occurs at the optic nerve head, where structural crowding of nerve fibers and reduction of the vascular supply may combine to impair perfusion to a critical degree and produce optic disc edema. The most common such syndrome is termed *anterior ischemic optic neuropathy* (AION) [95]. Generally, AION is categorized as either arteritic (associated with temporal arteritis) or nonarteritic (Table 6.7). Optic nerve ischemia affects the intraorbital portion of the nerve less frequently, with no visible disc edema, and this has been termed posterior ischemic optic neuropathy.

A number of syndromes that share similar characteristics also may be ischemic in origin, such as diabetic papillopathy.

Table 6.7 Comparison of arteritic versus nonarteritic anterior ischemic optic neuropathy (AION)

Feature	Arteritic AION	Nonarteritic AION
Age (mean years)	70	60
Sex ratio	Female > male	Male = female
Associated symptoms	Headache, scalp tenderness, jaw claudication	Pain occasionally noted
Visual acuity	Up to 76% < 20/200 (6/60)	Up to 61% > 20/200 (6/60)
Disc	Pale > hyperemic edema	Hyperemic > pale edema
	Cup normal	Cup small
Mean erythrocyte sedimentation rate (mm/hour)	70	20–40
Fluorescein angiogram	Disc and choroid filling delay	Disc filling delay
Natural history	Improvement rare	Improvement in up to 43%
	Fellow eye in up to 95%	Fellow eye in < 30%
Treatment	Corticosteroids	None proved

6.4.2 Anterior Ischemic Optic Neuropathy (AION)

6.4.2.1 Epidemiology and Pathogenesis

Nonarteritic anterior ischemic optic neuropathy (NAION) is the most common acute optic neuropathy in patients over 50 years of age, with an estimated annual incidence in the United States of 2.3–10.2 per 100000 population [96, 97]. The disease occurs more common in White than in Black or Hispanic populations [62, 96]. The incidence of arteritic anterior ischemic optic neuropathy (AAION) is significantly lower (0.36 per 100000 population annually in patients over 50 years of age [96]).

Arteritic Anterior Ischemic Optic Neuropathy

Studies have shown that AAION results from short posterior ciliary artery (SPCA) vasculitis and the resultant optic nerve head infarction. Human autopsy studies of acute AAION demonstrate optic disc edema with ischemic necrosis of the prelaminar, laminar, and retrolaminar portions of the nerve and infiltration of the SPCAs by chronic inflammatory cells. Segments of these vessels in some cases were occluded by inflammatory thickening and thrombus [98].

Fluorescein angiographic data support the histopathological evidence of involvement of the SPCAs in AAION [99]. There is a delayed filling of the optic disc and choroid. Poor or absent filling of the choroid has been depicted as a characteristic of AAION and can be used to differentiate AAION from NAION. Delayed completion of choroidal fluorescein filling that averages 30–69 s has been reported in AAION, compared with a mean of 5–13 s in NAION [100, 101].

Nonarteritic Anterior Ischemic Optic Neuropathy

NAION had been implicated to be a vascular event, but the direct evidence remains limited [102]. Histopathological studies showed laminar and retrolaminar infarction. Knox et al. have documented cavernous degeneration within ischemic regions of the optic nerve head, with distortion of adjacent axons, theorizing that this process may be responsible for the progressive course in some cases [103]. Periodic nocturnal systemic hypotension and the location of the optic disc in a watershed zone between distributions of lateral and medial SPCAs may be contributing factors [104].

Fluorescein angiographic studies in NAION suggest impaired optic disc perfusion. Detailed quantitative analysis of prelaminar optic disc and peripapillary choroidal filling in NAION confirms significantly delayed disc filling when compared with age-matched controls [105]. Delay in a segment of disc (Fig. 6.12) was present in 75.6% of such cases [106]. On the other hand, peripapillary choroidal filling was not delayed consistently and not significantly more than the degree of segmental delay often found in normal subjects. These findings suggest that the impaired flow to the optic nerve head in NAION is distal to the SPCAs, possibly at the level of the paraoptic branches that supply the optic nerve head directly.

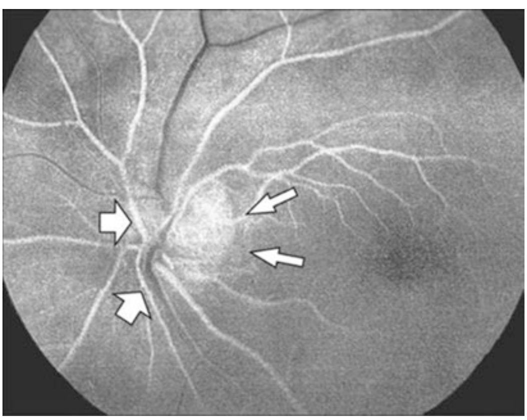


Fig. 6.12 Fluorescein angiogram, early arteriovenous phase, in nonarteritic anterior ischemic optic neuropathy. The temporal portion of the optic disc fills normally (small arrows), but the other areas demonstrate markedly delayed filling (large arrows) approximately 10 s later

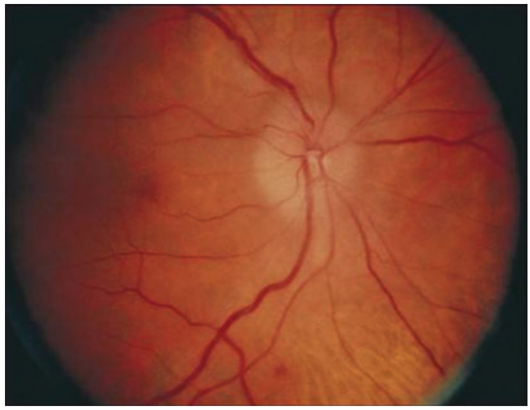


Fig. 6.13 Fundus view, anterior ischemic optic neuropathy. The optic disc demonstrates pale, diffuse edema

6.4.2.2 Ocular Manifestations

Patients with AION present with acute, painless, unilateral vision loss. The degree of visual loss varies widely, from minimal loss to no light perception, and the visual field loss corresponds to any pattern of deficit related to the optic disc. An altitudinal field defect is most common, but generalized depression, broad arcuate scotomas, and cecocentral defects also are seen. A relative afferent pupillary defect is present with monocular optic neuropathy. The optic disc edema is evident, followed by progressive visual loss for weeks to months [107]. A pale optic nerve disc edema is the hallmark of AION (Fig. 6.13). Hyperemic optic nerve swelling can also be seen (Fig. 6.14), particularly in the nonarteritic form. Flame hemorrhages are typically located adjacent to the disc, and the peripapillary retinal arterioles frequently are narrowed.

Arteritic Anterior Ischemic Optic Neuropathy

In 5–10% of cases, AION may occur as a manifestation of the vasculitis associated with temporal arteritis. Patients with the arteritic form usually note other symptoms of the disease – headache (most common), jaw claudication, and temporal artery or scalp tenderness are those that aligned most frequently with a final diagnosis of temporal arteritis. Malaise, anorexia, weight loss, fever, proximal joint arthralgia, and myalgia also are noted commonly; however, the disease occa-

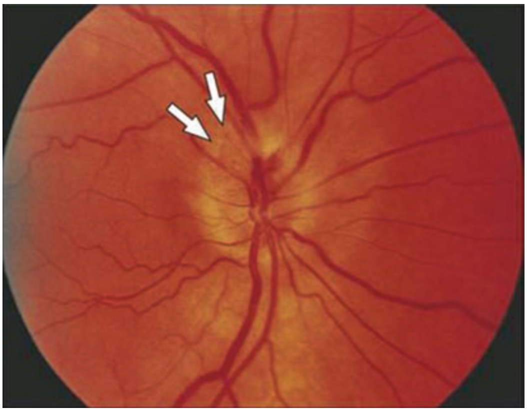


Fig. 6.14 Fundus view, nonarteritic anterior ischemic optic neuropathy. The hyperemic disc edema is more prominent superiorly. Focal surface telangiectasia of disc vessels is seen superotemporally (arrows)

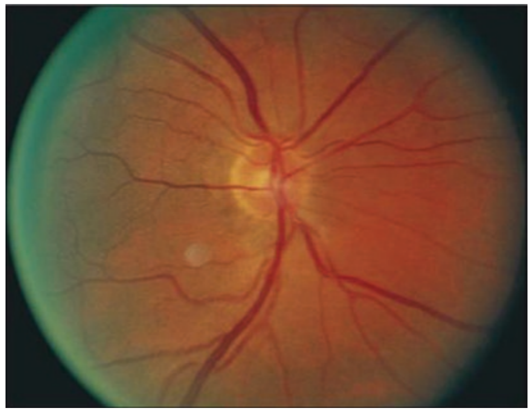


Fig. 6.15 Fellow eye in nonarteritic anterior ischemic optic neuropathy. The optic disc is small in diameter, with absent physiological cup and slight blurring of the nasal margin

sionally manifests with visual loss in the absence of overt systemic symptoms, so-called occult temporal arteritis.

Typically, AAION develops in elderly patients, with a mean age of 70 years, with severe visual loss (visual acuity < 20/200 (6/60) in the majority). It may be preceded by transient visual loss similar to that of carotid artery disease; this finding is extremely unusual in the nonarteritic form and, when present, is highly suggestive of arteritis [108]. Pallor, which may be severe, chalky white, is associated with the edema of the optic disc more frequently in AAION than in the nonarteritic form. Choroidal ischemia may be associated with the optic neuropathy and produces peripapillary pallor and edema deep to the retina. The disc of the fellow eye is of normal diameter most frequently, with a normal physiological cup (see NAION below) [109].

Nonarteritic Anterior Ischemic Optic Neuropathy

In 90–95% of cases, AION is unrelated to temporal arteritis. The nonarteritic form of the disease occurs in a relatively younger age group (mean age of 60 years) and usually is associated with less severe visual loss. Frequently, visual impairment is reported upon awakening, possibly related to nocturnal systemic hypotension [104]. The initial course of visual loss may be static (with little or no fluctuation of visual level after the initial loss) or progressive (with either episodic or visual loss that declines steadily over weeks to months prior to eventual stabilization). The progressive form has been reported in 22% [110] to 37% [111] of NAION cases. Usually, no associated systemic symptoms occur, although periorbital pain is described occasionally. Fellow eye involvement is estimated to occur in 12–19% by 5 years after onset [112]. Recurrent episodes of visual loss that result from NAION in the same eye are unusual and occur most often in younger patients.

The optic disc edema in NAION may be diffuse or segmental, hyperemic, or pale, but pallor occurs less frequently than it does in AAION. A focal region of more severe swelling often is seen and typically displays an altitudinal distribution, but it does not correlate consistently with the sector of visual field loss [105]. Diffuse or focal telangiectasia (Fig. 6.14) of the edematous disc may be present. The optic disc in the contralateral eye typically is small in diameter and demonstrates a small or absent physiological cup [109]. The disc appearance in such fellow eyes (Fig. 6.15) has been described as the *disc at risk*, with crowding of the axons at the level of the cribriform plate, mild disc elevation, and disc margin blurring without obvious edema.

6.4.2.3 Diagnosis and Ancillary Testing

The most important early step in the management of AION is the differentiation of the arteritic from the nonarteritic form of the disease. Measurement of the erythrocyte sedimentation rate (ESR) is standard. Active temporal arteritis usually is associated with an elevation of ESR to 70–120 mm/hour, and in acute AION that is associated with other typical features, this finding suggests the arteritic form; in most cases, it should prompt immediate corticosteroid therapy and confirmatory temporal artery biopsy (see below). The test has significant limitations, however, with normal measurements found in an estimated 16% of biopsy-proved cases [113]. Conversely, abnormally high readings occur normally with increasing age and with other diseases, most commonly occult malignancy, other inflammatory diseases, and diabetes. Measurement of serum C-reactive protein (CRP), another acute-phase plasma protein, may aid in the diagnosis. Hayreh et al. [114] reported 97% specificity for temporal arteritis in cases of AION in which both ESR >47mm/hour and CRP >2.45 mg/dL were found.

Confirmation of the diagnosis of temporal arteritis by superficial temporal artery biopsy is recommended in any case of AION in which a clinical suspicion of arteritis exists based on age, associated systemic symptoms, severity of visual loss, and elevated ESR and CRP levels. Positive biopsy findings, such as intimal thickening, internal limiting lamina fragmentation, and chronic inflammatory infiltrate with giant cells, provide support for long-term systemic corticosteroid therapy (Fig. 6.16). A negative biopsy result, however, does not rule out arteritis; both discontinuous arterial involvement ("skip lesions") and

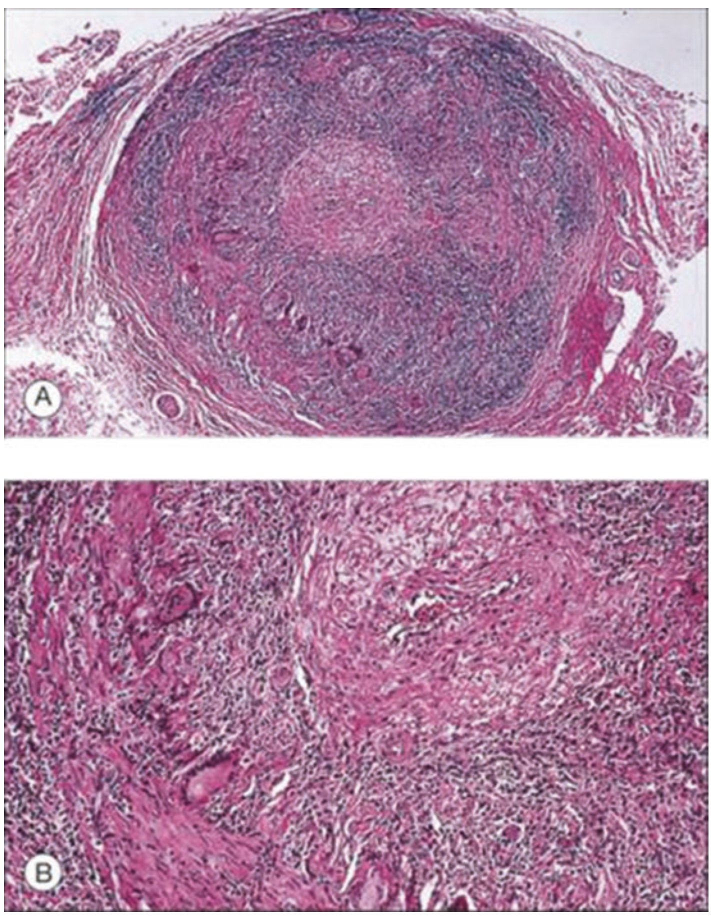


Fig. 6.16 Typical temporal arteritis. (**a**) Histological section shows a vasculitis involving all coats of the temporal artery. (**b**) Increased magnification shows the typical giant cell granulomatous inflammation

solely contralateral temporal artery inflammation may result in false-negative results. In the face of negative initial biopsy, consideration is given to contralateral biopsy in cases with high clinical suspicion of temporal arteritis. Recent reports indicate a 3–5% false-negative error rate [115].

6.4.2.4 Differential Diagnosis

The differential diagnosis of AION includes idiopathic optic neuritis, particularly in patients under 50 years of age; other forms of optic nerve inflammation, such as those related to syphilis or sarcoidosis; infiltrative optic neuropathies; anterior orbital lesions that produce optic nerve compression; and diabetic papillopathy. Optic neuritis may resemble AION with regard to clinical signs and symptoms such as the rate of onset, pattern of visual field loss, and optic disc appearance. However, the patient's age, lack of pain with eye movement, and pallor or segmental configuration of the disc edema enable differentiation. Early disc filling delay on fluorescein angiography may confirm ischemia. Syphilitic or sarcoid-associated optic neuritis often is associated with other intraocular inflammatory signs, which should prompt further testing. Orbital lesions typically produce gradually progressive visual loss. Associated signs of orbital disease, such as mild exophthalmos, lid abnormalities, or eye movement limitation, may suggest the use of neuroimaging to detect anterior orbital inflammation or tumor.

6.4.2.5 Systemic Associations

NAION is associated with a number of diseases that could predispose to reduced perfusion pressure or increased resistance to flow within the optic nerve head. Systemic hypertension has been documented in up to 47% of patients who have NAION [116] and diabetes in up to 24% [116]. Repka et al. [117] indicated that the prevalences of both hypertension and diabetes are increased over those of the control population in NAION patients in the age range 45–64 years but that in patients over 64 years of age, no significant difference exists from those of the general population. Diabetics in particular show a predisposition to NAION at a young age.

Carotid occlusive disease, itself, does not appear to be associated directly with NAION in most cases. However, indirect evidence shows increased central nervous system, small vessel, ischemic disease in patients who have NAION, based on magnetic resonance imaging (MRI) data [118]. Early reports did not indicate that the incidence of prior or subsequent cerebrovascular or cardiovascular events is increased, but more recent studies indicate that they are both more common than in the normal population, particularly in patients who have hypertension or diabetes [119]. Subsequent mortality, however, is not affected [119].

Also, NAION has been reported in association with multiple forms of vasculitis, acute systemic hypotension, migraine, optic disc drusen, and idiopathic vaso-occlusive diseases. Other risk factors, such as hyperopia, smoking, the presence of human lymphocyte antigen A29, and hyperlipidemia, have been proposed. Recent reports of the association of hyperhomocysteinemia with AION, particularly in patients under 50, are inconclusive [120]. Prothrombotic risk factors, such as protein C and S and antithrombin III deficiencies, factor V Leiden mutation, and cardiolipin antibodies, do not seem to be associated with AION [121].

6.4.2.6 Treatment

Arteritic Anterior Ischemic Optic Neuropathy

Early treatment of AAION is essential and must be instituted immediately in any suspected case of temporal arteritis. High-dose systemic corticosteroids are standard; the use of intravenous methylprednisolone at 1g/day for the first 3 days has been recommended for AAION when the patient is in the acute phase of severe involvement, because this mode of therapy produces higher blood levels of medication more rapidly. Oral prednisone in the range of 60–100 mg/day may be used initially and for follow-up to intravenous pulse therapy; alternate day regimens do not suppress the disease effectively. Treatment usually reduces systemic symptoms within

several days. A positive response is so typical that if it does not occur, an alternate disease process should be considered. Treatment is usually continued at high dose for several months before beginning taper.

Nonarteritic Anterior Ischemic Optic Neuropathy

There is no proven effective therapy for NAION. Oral corticosteroids at standard dosage (1 mg/kg per day) are not beneficial, and megadose intravenous therapy has not been evaluated systematically. Optic nerve sheath decompression (ONSD) surgery has been attempted, based on the theory that reduction of perineural subarachnoid cerebrospinal fluid pressure might improve local vascular flow or axoplasmic transport in the optic nerve head and thus reduce tissue injury in reversibly damaged axons. The Ischemic Optic Neuropathy Decompression Trial compared ONSD surgery in 119 patients with no treatment in 125 controls [62]. The study revealed no significant benefit for treatment and a possible, although not proven, harmful effect; it was recommended that ONSD not be performed for NAION. Hyperbaric oxygen, by marked elevation of the dissolved oxygen content in the blood, provides increased tissue oxygenation that might reduce damage in reversibly injured axons. A controlled clinical pilot study of hyperbaric oxygen in 22 patients who had acute NAION, however, has shown no beneficial effect [122]. Johnson et al. [123] reported a beneficial effect for oral levodopa on the visual outcome for NAION, but the study was controversial [124], and the effect is considered unproved. Neuroprotective agents have shown a beneficial effect in animal models of optic nerve damage, but are not proven to be effective in NAION. The effect of aspirin in reducing risk of fellow eye involvement is unclear [125, 126].

6.4.2.7 Course and Outcome

Arteritic Anterior Ischemic Optic Neuropathy

The major goal of therapy in AAION is to prevent visual loss in the fellow eye. If untreated, such involvement occurs in 54–95% of cases, [127, 128] typically within 4 months. With corticosteroid therapy, the rate of such breakthrough is reduced to an estimated 13%. Prognosis for visual recovery in the affected eye that has treatment generally is poor, but recent reports suggest a 15–34% improvement rate, [127, 129] which is higher with intravenous than with oral therapy. Worsening of vision in spite of therapy has been reported in 9–17% of cases [127, 129].

Nonarteritic Anterior Ischemic Optic Neuropathy

The course of untreated NAION varies considerably. Reports indicate that 24–43% of cases demonstrate spontaneous improvement of visual acuity by three Snellen lines or more [62, 110]. Even in the progressive form, improvement has been reported to occur in roughly 30%. Whether NAION is static or progressive, visual acuity and field stabilize after several months. Within 6 weeks, occasionally sooner, the optic disc becomes visibly atrophic, either in a sectorial (Fig. 6.17) or diffuse pattern. Further progression or recurrent episodes are extremely rare after 2 months and, if present, should prompt evaluation for another cause of optic neuropathy.

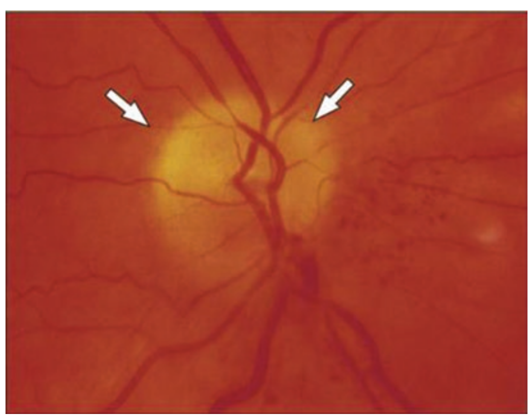


Fig. 6.17 Optic disc in nonarteritic anterior ischemic optic neuropathy. The disc, 2 months after onset of inferior visual field loss, is segmentally atrophic superiorly (arrows), with sparing and resolving edema inferiorly

6.4.3 Posterior Ischemic Optic Neuropathy

Ischemia of the optic nerve that does not involve the optic nerve head is termed posterior ischemic optic neuropathy (PION). It presents with acute visual loss associated with signs of optic neuropathy (afferent pupillary defect and visual field loss) in one or both eyes, with initially normal appearance of the optic disc, which subsequently becomes atrophic.

The diagnosis of PION is most often made in one of two settings:

- Vasculitis, most importantly giant cell arteritis (GCA); evaluation for GCA should be the primary consideration with this presentation in the elderly.
- The combination of systemic hypotension and anemia, usually related to blood loss either from surgery (coronary artery bypass and lumbar spine procedures most commonly) [130], gastrointestinal bleed, or trauma.

The differential diagnosis includes compressive, inflammatory, and infiltrative optic neuropathies, although the onset in PION is typically more abrupt. In most cases, neuroimaging is indicated to rule out these possibilities.

Sadda et al. reported a multicenter, retrospective review of 72 patients with PION, adding a third classification paralleling the nonarteritic form of AION [131]. The nonarteritic PION group accounted for 38 of the 72 patients, exhibited similar risk factors, and followed a clinical course precisely like that of NAION. In contrast to perioperative and arteritic PION, which was characterized by severe visual loss with little or no recovery, nonarteritic PION was less severe and showed improvement in 34% of patients. It is important to recognize this nonarteritic form in patients with acute optic neuropathy but no optic disc edema, a scenario that may be mistaken for retrobulbar optic neuritis. Such patients, particularly those with ischemic white matter lesions on MRI, might be incorrectly begun on immunomodulatory therapy to reduce the risk of MS [132]. PION differs from optic neuritis by its occurrence in older age groups, with lack of pain on eye movements.

6.4.4 Diabetic Papillopathy

6.4.4.1 Pathogenesis

The pathogenesis of diabetic papillopathy is unclear. Early investigators postulated either a toxic effect on the optic nerve secondary to abnormal glucose metabolism or a vascular disturbance of the inner disc surface, similar to that which produces retinal edema, with the resultant microvascular leakage into the disc. The most commonly proposed theory suggests diabetic papillopathy to be a mild form of NAION, with reversible ischemia of both the prelaminar and inner surface layers of the optic nerve head [133]. Edema of the optic nerve head in the absence of significant visual dysfunction and not secondary to elevated intracranial pressure occurs in several presumed vascular disorders as follows:

- Asymptomatic optic disc edema, which evolves to typical NAION weeks to months after initial symptoms [107]
- Asymptomatic disc edema of the fellow eye in patients who have NAION, which may either progress to NAION or resolve spontaneously
- Disc edema in association with systemic hypertension, which resolves without sequelae as blood pressure is normalized

Diabetic papillopathy fits this category, as well. The prominent surface telangiectasias may represent vascular shunting from prelaminar to ischemic vascular beds. The frequent occurrence of a crowded optic disc in the fellow eye (see below) [134], as in NAION, also supports an ischemic mechanism.

6.4.4.2 Ocular Manifestations

Early reports of diabetic papillopathy depicted the acute onset of unilateral or bilateral disc edema in young, type 1 diabetics, without the usual defects in visual field and pupillary function associated with NAION or optic neuritis; [133, 135] a recent report included a substantial

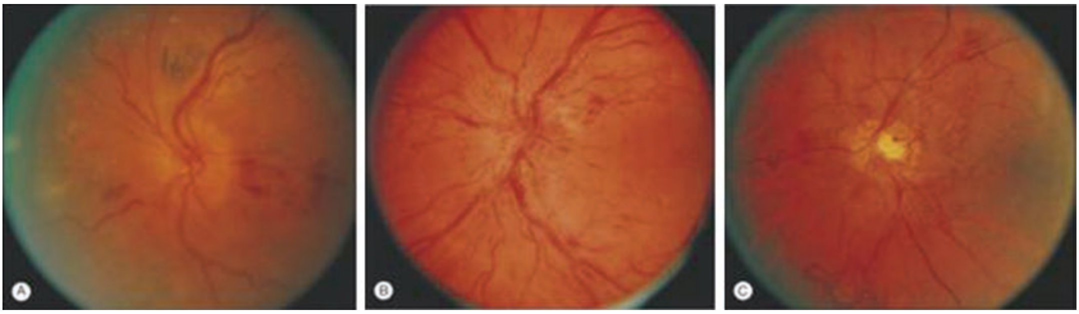


Fig. 6.18 Optic disc in diabetic papillopathy. (**a**) Nonspecific hyperemic disc edema. (**b**) Surface vessels show marked telangiectasia, in which dilated vessels generally follow a radial distribution. (**c**) Contrast with diabetic optic disc neovascularization; note the irregular, random branching pattern of surface vessels

number of older patients with type 2 diabetes [134].

The currently accepted criteria for the diagnosis of diabetic papillopathy include:

- Presence of diabetes (approximately 70% type 1, 30% type 2)
- Optic disc edema (unilateral in roughly 60%)
- Only mild optic nerve dysfunction

The absence of ocular inflammation or elevated intracranial pressure also is essential to the diagnosis.

Although younger patients predominate (approximately 75% of those reported are under the age of 50 years), those affected may be of any age and typically experience either no visual complaints or vague, nonspecific visual disturbance, such as mild blurring or distortion; transient visual obscuration has been reported rarely. Visual acuity is usually only mildly impaired; over 75% of reported cases measured 20/40 (6/12) or better. Macular edema contributes to visual acuity loss in many cases. Pain is absent, as are other ocular or neurological symptoms.

The involved optic discs may demonstrate either nonspecific hyperemic edema or, in approximately 55% of cases, marked telangiectasia of the inner surface microvasculature (Fig. 6.18 a, b); pale swelling typically has been a criterion for exclusion and suggests AION. The surface telangiectasia is so prominent in many cases that it may be mistaken for neovascularization (Fig. 6.18c).

True disc neovascularization occasionally is superimposed on the edema of diabetic papillopathy. The fellow eye frequently demonstrates crowding, with a small cup-to-disc ratio similar to the configuration seen in patients who have NAION [134].

Diabetic retinopathy usually is present (in more than 80% of reported cases) at the time of onset of papillopathy, but it varies in severity. It is associated with cystoid macular edema in about 25% of cases and neovascularization in approximately 9%.

6.4.4.3 Differential Diagnosis

Conditions that may simulate diabetic papillopathy include papilledema (elevated intracranial pressure), hypertensive papillopathy, optic disc neovascularization, papillitis, and NAION. Symptoms of elevated intracranial pressure usually differentiate papilledema, and in bilateral cases with such symptoms, neuroimaging and lumbar puncture must be considered. Disc edema related to systemic hypertension typically does not demonstrate prominent telangiectasia and usually is associated with hypertensive retinopathy; blood pressure measurement is important in suspected cases. Papillitis and NAION both demonstrate significant optic nerve dysfunction, as evidenced by afferent pupillary defect and visual field loss.

6.4.4.4 Course and Outcome

Although systemic corticosteroids have been used in isolated cases, no proven therapy exists

for this disorder. If untreated, the optic disc edema gradually resolves over a period of 2–10 months, to leave minimal optic atrophy in about 20% of cases and subtle, if any, visual field loss. Visual acuity at the time of resolution of edema is 20/40 (6/12) or better in about 80% of cases; the remainder of patients suffer visual impairment because of maculopathy. The long-term visual prognosis for patients who have diabetic papillopathy, however, is limited by the associated diabetic retinopathy. Proliferative changes, with attendant complications, develop in approximately 25% of cases.

6.5 Traumatic Optic Neuropathies

6.5.1 Introduction

The optic nerve may be damaged directly or indirectly after head trauma. Both direct and indirect injuries may damage the optic nerve as a result of transection of nerve fibers, interruption of blood supply, or secondary hemorrhage and edema. Primary injury to the optic nerve fibers by transection or infarction at the time of injury results in permanent damage.

6.5.2 Epidemiology and Pathogenesis

Indirect injury to the optic nerve occurs in 0.5–5% of patients who suffer closed head trauma [136]. The optic nerve may be damaged by shearing and avulsion of its nutrient vessels or by pressure transmitted along the bone to the optic canal.

6.5.3 Ocular Manifestations

Patients with traumatic optic neuropathy present with decreased visual acuity, visual field defects, and a relative afferent pupillary defect. If a relative afferent pupillary defect is not evident, the patient does not have a traumatic optic neuropathy, unless it is bilateral. Patients who have bilateral optic nerve dysfunction demonstrate light-near dissociation of their pupillary reactions. The near response is brisker than the pupillary response to light.

If the anterior optic nerve is injured, infarction, hemorrhage, or a central retinal artery occlusion is evident on fundus exam. Patients who have a more posterior injury to the nerve may be found to have a normal fundus on examination but have an afferent pupillary defect and visual loss.

6.5.4 Diagnosis and Ancillary Testing

Computed tomography (CT) is the diagnostic procedure of choice. Treatable causes of optic nerve compression, such as orbital and optic nerve sheath hemorrhages, are detected using CT scans; [137] CT scan also detects orbital and optic canal fractures. The presence of an optic canal fracture is not necessary for the diagnosis of traumatic optic neuropathy.

6.5.5 Differential Diagnosis

The differential diagnosis should include other causes of optic neuropathies, as well as causes of obviously treatable optic nerve compression (Table 6.8).

6.5.6 Pathology

The optic nerve is most commonly injured at the intracanalicular and intracranial portion. Forces applied to the frontal bone may be transmitted

Table 6.8 Differential diagnosis of traumatic optic neuropathy

Optic nerve sheath hematoma	Optic nerve inflammation
Orbital hematoma	Orbital inflammation
Subperiosteal hematoma	Sinusitis with orbital involvement
Coincident optic neuropathies	Ischemic optic neuropathy
Compression by tumor or aneurysm	Optic neuritis

and concentrated at the optic canal [138]. Acceleration and deceleration forces may cause a partial or total avulsion of the retrobulbar optic nerve or contusion necrosis and avulsion of the vascular supply of the intracanalicular optic nerve. The intracranial optic nerve may be injured by the falciform dural fold caused by the force of a shifting brain at the moment of impact [137].

Optic nerve injuries may be caused by primary and secondary mechanisms. A review of such mechanisms was published [137]. Treatment consists of attempts to limit secondary injury and salvage axons that survive the initial trauma.

6.5.7 Treatment

Visual loss and a relative afferent pupillary defect that accompany an orbital hemorrhage warrant immediate decompression by either drainage of the hemorrhage or lateral canthotomy or cantholysis or both. Prompt surgical decompression of the optic nerve sheath may restore visual function [139]. The primary injuries to optic nerve are not treatable, whereas the secondary effects of the primary injury, edema and hemorrhage, may be treatable.

Treatment of traumatic optic nerve injuries with high-dose corticosteroids is based upon the success attained in treatment of spinal cord injuries [140]. Administered within 8 h after injury, high-dose corticosteroids have an antioxidant and membrane-stabilizing effect that limits secondary cell damage and increases microcirculatory perfusion [141]. After 8 h, corticosteroids have little effect on the biochemical dynamics of the injured axon. Surgical removal of the bony wall of the optic canal relieves compression of the optic nerve and may allow it to regain function. Unfortunately, these proposed treatments limit secondary injuries only. Axons damaged terminally do not regenerate – their visual function is often irretrievably lost.

If possible, treatment should be initiated as soon as possible. Methylprednisolone 30 mg/kg is administered intravenously over 30 min, followed by 15 mg/kg 2 h later. Treatment is continued with 15 mg/kg every 6 h for 24–48 h. If visual function improves, the corticosteroids are tapered rapidly. If visual function deteriorates as corticosteroids are tapered, optic canal decompression may be offered. Patients who do not respond to corticosteroid treatment may be considered candidates for optic canal decompression.

6.5.7.1 Course and Outcome

Currently no standard of care exists for the management of patients with traumatic optic neuropathies [139, 142]. Several studies show that patients treated with corticosteroids or a combination of corticosteroids and extracranial optic canal decompression seem to have better visual prognosis than untreated patients [143–145]. Treatment with high-dose corticosteroids seems to improve vision more quickly than treatment with high-dose intravenous corticosteroids, but there is no significant difference in the final visual outcome [146–148]. Some suggest that treatment may even be harmful based on a recent study of head injury patients where the steroid-treated group had a greater mortality [149]. Patients may improve spontaneously without treatment [143], but treated patients appear to have a better visual prognosis [143–145].

6.6 Rhegmatogenous Retinal Detachment

6.6.1 Introduction

Rhegmatogenous retinal detachments are important causes of visual loss, particularly in the patients who are at risk for retinal tears. Timely recognition of the clinical symptoms and signs of retinal detachment is crucial for correct diagnosis and to maximize the chances of a favorable surgical outcome to preserve vision.

6.6.2 Epidemiology and Pathogenesis

The characteristic pathogenesis of rhegmatogenous retinal detachment is vitreous liquefaction

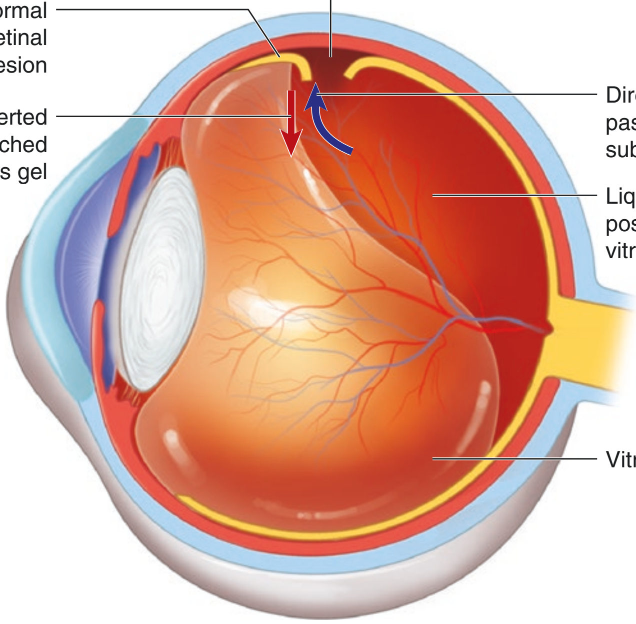


Fig. 6.19 Classical pathogenesis of rhegmatogenous retinal detachment. The detached vitreous gel has caused a retinal tear by exerting traction upon the retina at the site of a vitreoretinal adhesion. Liquid in the vitreous cavity passes through the break into the subretinal space

followed by a posterior vitreous detachment (PVD), which in turn causes retinal tears at the sites of significant vitreoretinal adhesions (Fig. 6.19). All ocular conditions that are associated with an increased prevalence of vitreous liquefaction and PVD or with an increased number or extent of vitreoretinal adhesions are associated with a higher incidence of retinal detachment.

6.6.2.1 Factors That Cause Retinal Detachment

The major factors associated with retinal detachment include retinal breaks, vitreous liquefaction and detachment, traction on the retina (vitreoretinal traction), and intraocular fluid currents associated with movement of liquid vitreous and subretinal fluid. The majority of eyes with retinal breaks do not develop retinal detachment because normal physiological forces keep the retina in place. Retinal detachment occurs when the combination of factors that promote retinal detachment overwhelms the normal attachment forces.

Retinal Breaks

Retinal breaks are classified as holes, tears, or dialyses. Retinal holes are full-thickness retinal defects that are not associated with persistent vitreoretinal traction in their vicinity. They usually occur as a result of localized atrophic intraretinal abnormalities.

Retinal tears are usually produced by PVD and subsequent vitreoretinal traction at sites of significant vitreoretinal adhesions (Figs. 6.19 and 6.20). Vitreous traction usually persists at the edge of a tear, which promotes progression of the retinal detachment.

Dialyses are linear retinal breaks that occur along the ora serrata. Although most are associated with blunt ocular trauma, dialyses can occur spontaneously.

Vitreous Liquefaction and Detachment

Posterior vitreous detachment (PVD) usually occurs as an acute event after significant liquefaction of the vitreous gel. The precipitating

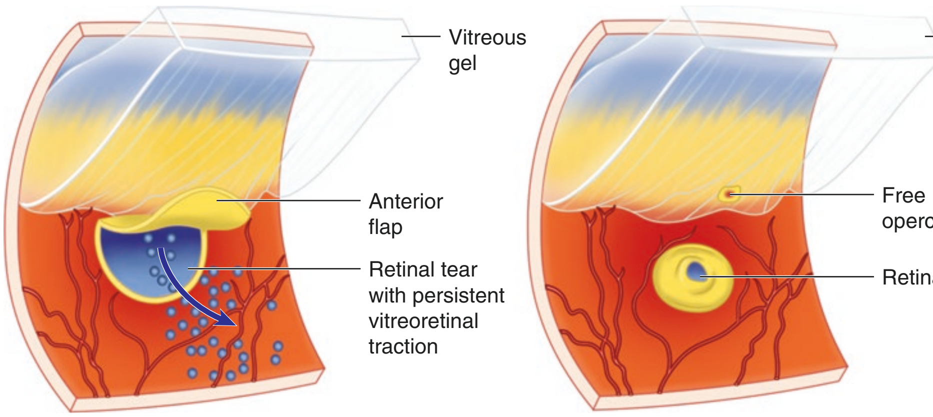


Fig. 6.20 Retinal detachment. Retinal tears are due to vitreoretinal traction. Persistent traction causes extensive retinal detachment (on left). If the traction results in a break that is not associated with persistent vitreoretinal traction (on right), the tear acts as a retinal hole, and detachment is quite unlikely

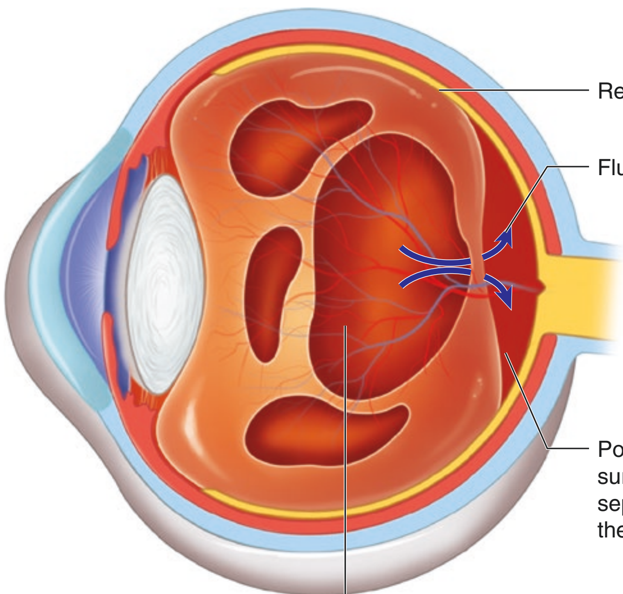


Fig. 6.21 Separation of the posterior cortical vitreous. In an acute event, posterior vitreous detachment usually begins with an apparent break in the cortical vitreous that overlies the macula. Fluid from a central lacuna flows through this hole and separates the cortical vitreous from the retina

event is likely a break in the posterior cortical vitreous in the region of the macula [150]. This is followed by the immediate passage of intravitreal fluid into the space between the cortical vitreous and retina (Fig. 6.21). Characteristically, this rapid movement of fluid and the associated collapse of the remaining structure of the gel result in extensive separation of the vitreous gel and retina posterior to the vitreous base, especially in the superior quadrants. Partial PVDs usually progress rapidly (within days) to become complete, although they do not always separate from the entire posterior retina.

Traction on the Retina

Vitreoretinal traction has a number of causes, which range from simple action of gravitational force on the vitreous gel to prominent transvitreal fibrocellular membranes. Gravitational force is important and probably accounts for the high

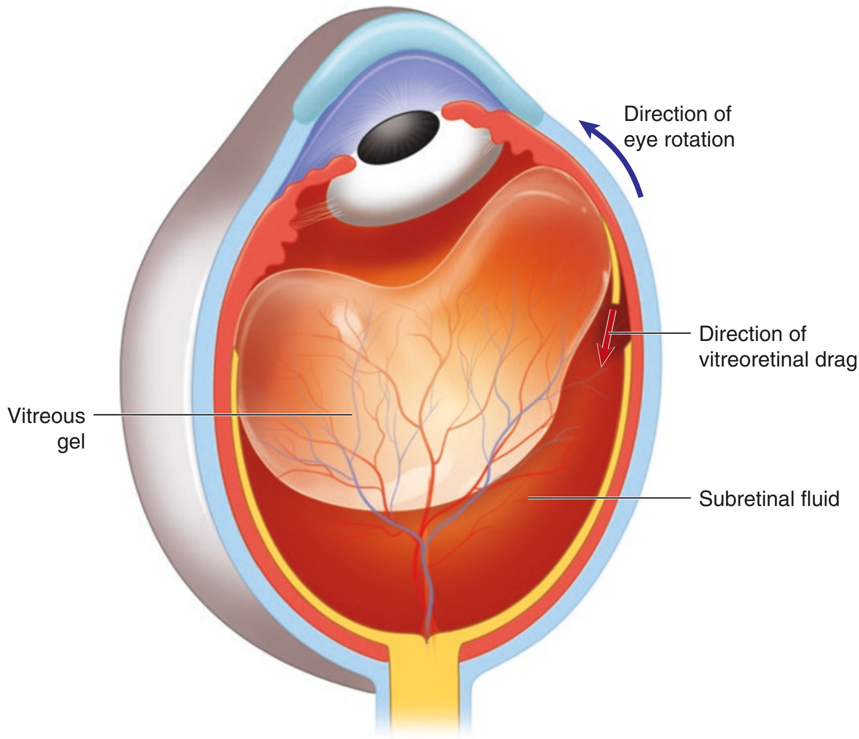


Fig. 6.22 Vitreoretinal traction caused by eye movements. When the eye rotates, the inertia of the vitreous gel causes it to lag behind the eye movement, which effectively causes vitreoretinal traction ("drag") in the opposite direction and the production of a retinal tear

percentage of superior retinal tears (80%). However, rotational eye movements, which exert strong forces on all vitreoretinal adhesions, are probably more important causes of ongoing vitreoretinal traction [151]. When the eye rotates, the inertia of the detached vitreous gel causes it to lag behind the rotation of the eye wall and, therefore, the attached retina. The retina at the site of a vitreoretinal adhesion exerts force on the vitreous gel, which causes the adjacent vitreous to rotate. The vitreous gel, because of its inertia, exerts an equal and opposite force on the retina, which can cause a retinal break or separate the neural retina farther from the pigment epithelium if subretinal fluid is already present (Fig. 6.22). When the rotational eye movement stops, the vitreous gel continues its internal movement and exerts vitreoretinal traction in the opposite direction.

In addition to gravitational and inertial forces, vitreoretinal traction can be caused by contracture of intraocular fibroproliferative tissue associated with trauma, retinal vascular proliferative disorders, and other conditions. This type of traction does not always create a retinal break. Instead, a traction retinal detachment may be produced. Sometimes significant vitreoretinal traction initially causes a localized traction detachment, which later becomes more extensive with the development of a retinal break.

Liquid Currents

Continuous flow of liquid vitreous through a retinal break into the subretinal space is necessary to maintain a rhegmatogenous retinal detachment. Rotary eye movements can cause liquid currents in the vitreous to push against the gel adjacent to the retinal break and to dissect beneath the edge of a retinal break into the subretinal space (Fig. 6.23). Subsequent eye movements also have an inertia effect on the subretinal fluid that favors extension of the retinal detachment (Fig. 6.24).

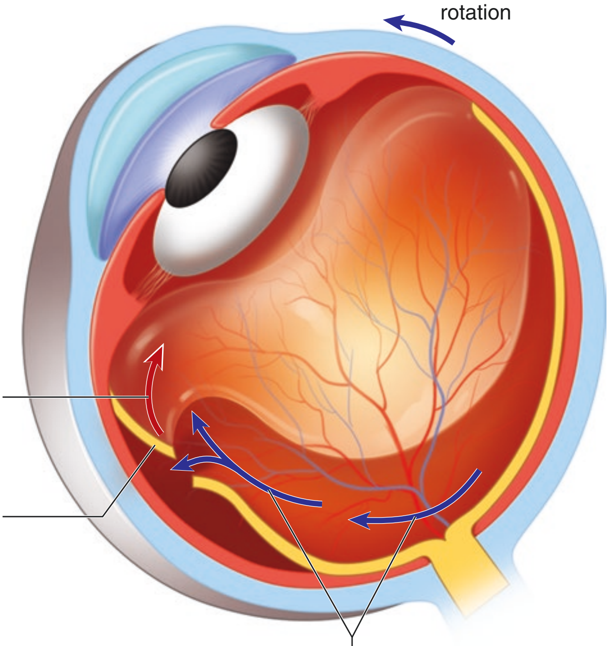


Fig. 6.23 Extension of retinal detachment associated with eye movements. Rotary eye movement causes movement of the vitreous gel, which increases traction upon the retinal break. In addition, liquid currents dissect beneath the edge of the retinal tear and push against the vitreous gel adjacent to the tear. All three factors promote extension of the retinal detachment

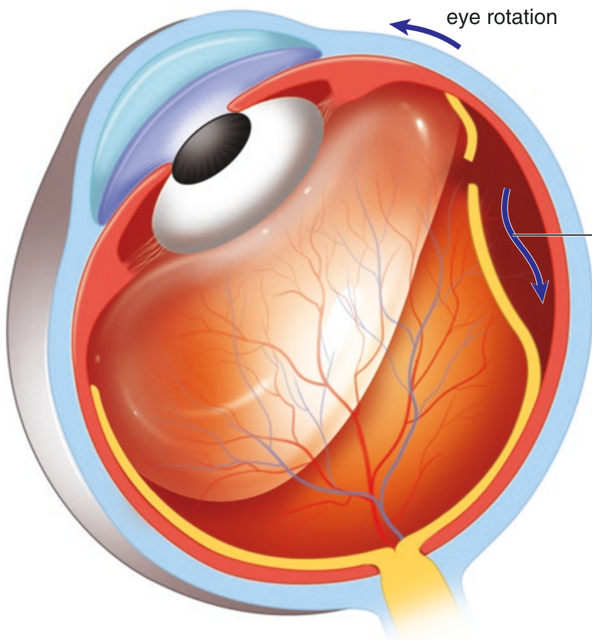


Fig. 6.24 Extension of subretinal fluid associated with eye movements. In addition to exacerbating vitreoretinal traction, rotary eye movements have an inertia effect upon subretinal fluid that causes it to dissect further between the retina and pigment epithelium

6.6.2.2 Conditions That Predispose an Eye to Retinal Detachment

Retinal detachments are relatively unusual in the general population – the accepted annual incidence figure is approximately 1:10 000 [152]. However, a variety of ocular and systemic disorders are associated with pathological vitreous liquefaction, premature vitreous detachment, and extensive sites of vitreoretinal adhesion. These conditions, therefore, are also associated with increased chances of retinal detachment. Particularly important predisposing entities include high myopia, pseudophakia and aphakia, blunt and penetrating ocular trauma, and cytomegalovirus retinitis associated with acquired immunodeficiency syndrome.

Although cataract surgery has been performed on only approximately 3% of the general population, up to 40% of eyes with retinal detachment have had prior cataract surgery [153]. Retinal detachment represents the most significant potential postsurgical complication of cataract surgery, as it occurs in nearly 1% of pseudophakic eyes [154]. Removal of the natural lens is believed to increase the risk of retinal detachment because of its effect on vitreous liquefaction and subsequent premature PVD. The status of the posterior capsule determines the rapidity of vitreous liquefaction. It is clear that opening the posterior capsule, either surgically or with a neodymium-doped yttrium-aluminum-garnet (Nd:YAG) laser, significantly increases the incidence of retinal detachment [155].

High myopia (> 6.0 D myopia) is associated with at least a threefold increased incidence of retinal detachment [156]. Severe ocular trauma is believed to be responsible for 10–15% of retinal detachments, and many patients with cytomegalovirus retinitis develop a rhegmatogenous retinal detachment with breaks at sites of prior inflammation.

Risk factors for retinal detachment are not mutually exclusive and may be additive. For example, prior cataract extraction and nonsurgical trauma are more likely to be complicated by retinal detachment in myopic eyes. Pathological vitreoretinal changes often occur bilaterally – patients who have a retinal detachment in one eye usually have a significantly increased risk of retinal detachment in the fellow eye, provided that additional acquired risk factors are comparable.

6.6.3 Ocular Manifestations

The early symptoms of acute retinal detachment are the same as those of acute PVD – the sudden onset of tiny dark floating objects, frequently associated with photopsia (flashes). Photopsia is usually brief, in the temporal visual field, and is best seen in the dark immediately following eye movement. Loss of visual field does not occur until sufficient fluid has passed through the retinal break(s) to cause a retinal detachment posterior to the equator. Retinal detachments with a relatively small amount of subretinal fluid (less than two disc diameters from the break) are often not accompanied by visual field loss; these are termed subclinical detachments. Rarely, but especially in young myopes, slowly progressive asymptomatic retinal detachments develop without PVD. This most commonly occurs temporally and inferiorly and secondary to atrophic holes in lattice degeneration [157].

The vast majority of retinal breaks are located at the equator or more anteriorly; subretinal fluid initially accumulates in the retinal periphery, where it causes a corresponding loss of peripheral vision in the area that is related inversely to the location of the retinal detachment (Fig. 6.25). The loss of peripheral vision (a “curtain effect”) increases as the detachment enlarges; central visual acuity is lost when subretinal fluid passes beneath the macula. Frequently, patients do not notice any symptoms until the macula becomes involved.

Retinal breaks associated with small amounts of subretinal fluid may be difficult to detect; however, the diagnosis becomes more obvious as the retinal detachment increases in size. A stereoscopic vitreoretinal examination typically reveals an elevated sensory retina in the area of detachment, but the critically important identification of all retinal breaks may remain difficult – it is considerably easier to diagnose the retinal detachment than to detect all retinal breaks.

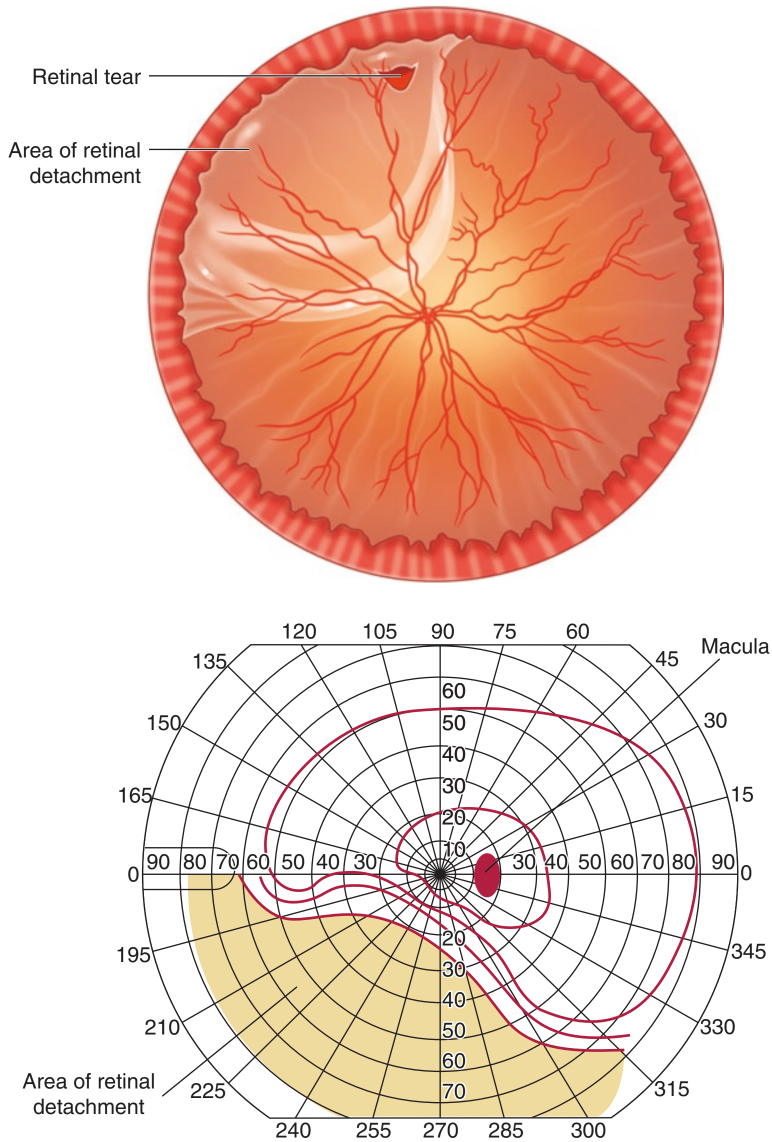


Fig. 6.25 Superotemporal rhegmatogenous retinal detachment. The neural retina is elevated in the area of detachment, and the macula remains uninvolved. Visual field defect associated with retinal detachment shows that peripheral vision is lost inferonasally, corresponding to the area of detachment. The visual defect is an inverted image of the retinal detachment

Owing to the effects of gravity, the topography of a retinal detachment is of major value in the prediction of the most likely locations of retinal breaks [158]. Retinal breaks are usually present superiorly within the area of detachment. Thus, if a retinal detachment involves one upper quadrant or both the superior and inferior quadrants on one side of the vertical meridian, the responsible retinal break is likely to be near the superior edge of the detachment (Fig. 6.26). Retinal detachments that involve the inferior quadrants tend to follow the same rules, but the progression of the detachment is often much slower, and symmetrical spread of subretinal fluid may occur on both sides of the break. Therefore, detachments that involve one or both inferior quadrants may have a break near a superior margin of the detachment or in the meridian that bisects the area of detachment (Fig. 6.27). Nevertheless, because multiple retinal breaks are common, the entire periphery of the detached retina must be meticulously examined.

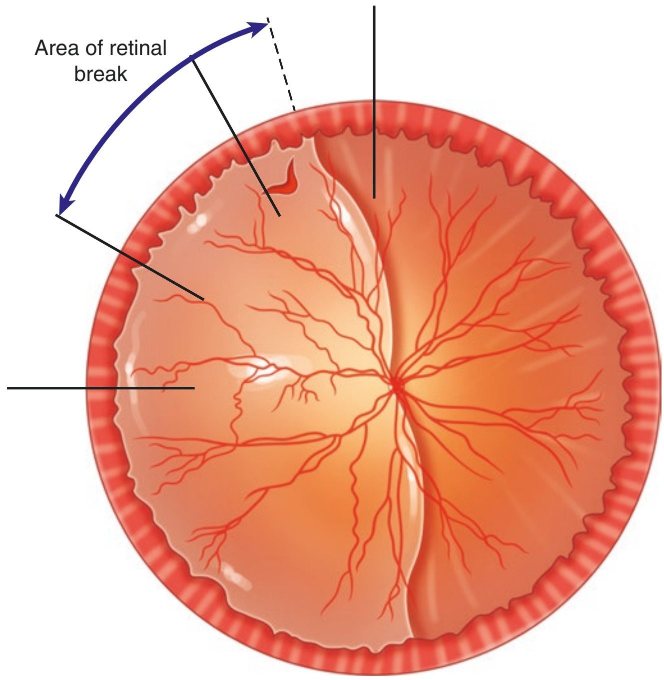


Fig. 6.26 Location of the retinal break. Retinal detachments that involve both quadrants on the same side of the vertical meridian are usually caused by a retinal break within 1–1.5 clock hours of the superior margin of the detachment

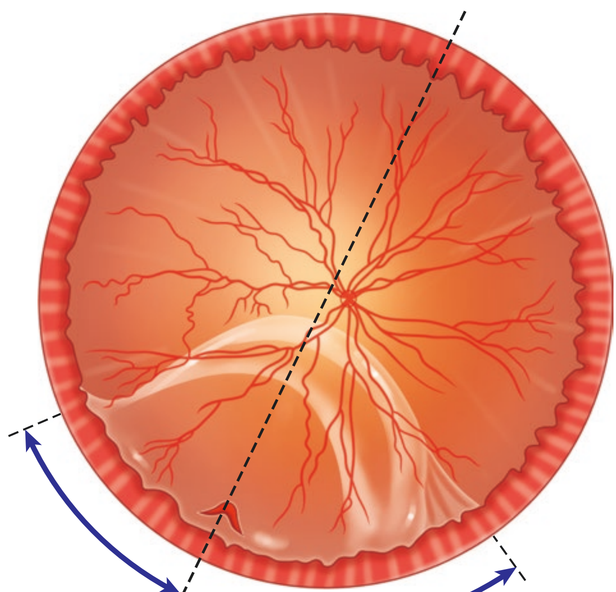


Fig. 6.27 Location of the retinal break. Retinal detachments that involve both lower quadrants but extend farther superiorly on one side are usually caused by a retinal break within 1–1.5 clock hours of the superior margin of the retinal detachment or by a break in a meridian that bisects the margins of the retinal detachment

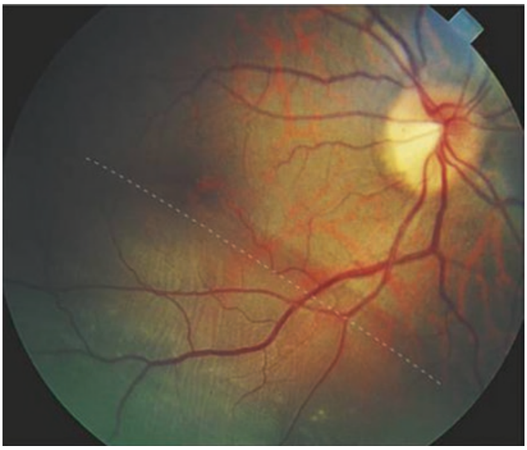


Fig. 6.28 Rhegmatogenous retinal detachment. The inferior temporal portion of the retina is detached, and the subretinal fluid makes visualization of the pigment epithelium and choroid relatively difficult

Table 6.9 Differential diagnosis of rhegmatogenous retinal detachment

Traction Retinal Detachment
Proliferative diabetic and other retinopathies
Following penetrating trauma
Exudative Retinal Detachment
Inflammatory disorders
Choroidal neoplasms
Retinal vascular tumors and other disorders
Retinoschisis
Age-related
Congenital sex-linked
Elevated Choroidal Lesions
Choroidal detachments
Choroidal tumors
Intravitreal Optical Illusions
Vitreous hemorrhage

6.6.4 Diagnosis

The diagnosis of rhegmatogenous retinal detachment is made on the basis of clinical examination. Ultrasonography can be used to assist in the diagnosis, especially in eyes with poor view to the posterior segment. The location and identification of the causative retinal breaks are based upon the configuration of the detachment as well as on the patient's history and associated findings.

The vast majority of retinal detachments are diagnosed easily with a binocular stereoscopic evaluation of the entire retina. Areas of retinal detachment are recognized by elevation of the neural retina from the RPE and loss of pigment epithelial and choroidal detail beneath the elevated retina (Fig. 6.28). Retinal breaks are also discovered by direct visualization. Indentation of the peripheral retina (scleral depression) is employed to facilitate visualization of the anterior retina at different angles, and this improves abilities to identify all retinal defects.

6.6.5 Differential Diagnosis

Retinal detachments that occur as a result of retinal breaks must be distinguished from other causes and retinoschisis (see Table 6.9). Choroidal lesions that elevate the overlying retina and intravitreal pathology that simulates an elevated retina may also be confused with retinal detachment.

The distinction between different types of retinal detachment can be difficult in eyes with small or undetectable retinal breaks and features associated with intraocular proliferation or exudation. In some cases, both a rhegmatogenous and a traction or exudative component may be important in the pathogenesis of the detachment. This is particularly common in eyes with proliferative diabetic retinopathy and retinal detachment. Pure traction detachments usually have a concave surface, and the shape, location, and extent of the detachment can be accounted for by the evident vitreous traction (Fig. 6.29). Diabetic retinal detachments with a rhegmatogenous component are usually more extensive and often have a convex contour (Fig. 6.30). Exudative detachments from a variety of causes are characterized by shifting subretinal fluid, which assumes a dependent position beneath the retina. In most cases, the fluid is located inferiorly, and its cause within or beneath the retina may be apparent (Fig. 6.31) or quite subtle.

6.6.6 Systemic Associations

Some systemic disorders are associated with rhegmatogenous retinal detachment. These conditions

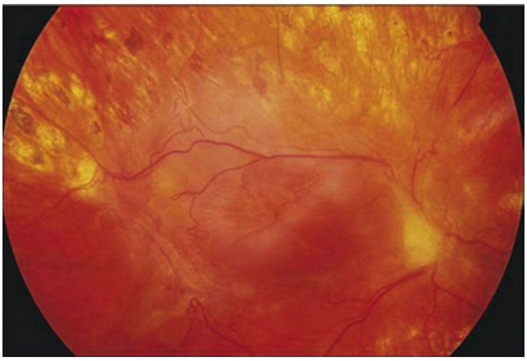


Fig. 6.29 Traction retinal detachment. The central area of retinal elevation is localized and due to areas of visible vitreoretinal traction associated with proliferative diabetic retinopathy

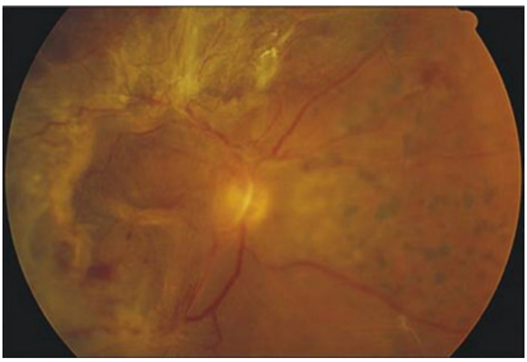


Fig. 6.30 Combined retinal detachment. Vitreoretinal traction associated with proliferative diabetic retinopathy has caused a tiny retinal break; the area of retinal elevation is more extensive and more convex than usually found in a pure traction detachment

Fig. 6.31 Exudative retinal detachment. The small amounts of subretinal fluid (note the retinal striae) are due to leakage from an inflammatory process that involves the choroid and retinal pigment epithelium

are either due to a hereditary systemic abnormality (usually an inherited disorder of collagen) or the result of complications of a systemic disease. The most important entity in the former group is Stickler's syndrome, in which a predisposition to retinal detachment is associated with a variety of facial and skeletal abnormalities. The most important systemic diseases associated with the complication of retinal detachment are diabetes mellitus and acquired immunodeficiency syndrome.

6.6.7 Pathology

The first visible pathological retinal changes associated with the retinal detachments occur in the outer segments of the photoreceptors [159]. Long-standing retinal detachments are associated with further atrophy of the photoreceptor layer and cystic degeneration within the retina [160]. The vitreous macromolecular changes that result in liquefaction of the gel have not been identified.

Successfully repaired retinal detachments show a variety of histopathological abnormalities. There is a high incidence of epiretinal membrane formation [161]. Cystoid macular edema is common as well, along with significant photoreceptor atrophy in many eyes.

6.6.8 Treatment

The main goal of retinal detachment surgery is to close each retinal break and to reattach the retina. Long-term closure of retinal breaks may require permanent reduction or elimination of vitreoretinal traction, accompanied by maneuvers designed to offset the harmful effects of fluid currents in the vitreous cavity.

Scleral buckling techniques and vitrectomy techniques are performed frequently to repair retinal detachments. Pneumatic retinopexy is the third technique that is frequently employed in selected cases [162]. Contemporary options in the management of primary rhegmatogenous retinal detachment are listed in Table 6.10.

Table 6.10 Options for the management of primary retinal detachment

Observation (Very rarely employed)
Laser Demarcation Permanent Scleral Buckle
Encircling with/without drainage
Segmental with/without drainage
Temporary Scleral Buckle
Lincoff balloon
Absorbable buckling materials
Pneumatic Retinopexy
Routine
With drainage of subretinal fluid or intravitreal liquid
Primary Vitrectomy
Combinations of the above techniques

6.6.9 Course and Outcome

Surgical success for the repair of rhegmatogenous retinal detachment has now improved significantly, and approximately 95% of all retinal detachments can be successfully repaired (i.e., the retina is returned to its normal anatomic position with no residual subretinal fluid). The three most common reasons for failure of retinal detachment surgery are:

- Failure to identify and/or close all retinal breaks
- New retinal breaks
- Proliferative vitreoretinopathy

Unfortunately, visual results after anatomically successful surgery do not reflect this high rate of anatomical success. Postoperative visual acuity is most dependent upon the extent of damage to the macula caused by the retinal detachment. If the macula becomes detached by subretinal fluid, permanent damage to vision usually occurs in spite of surgical reattachment. In eyes with no macular detachment present, 90% can be expected to have 20/40 vision or better following surgery. On the other hand, about 10% of eyes with normal vision have some visual loss after successful repair of a macula-sparing detachment [163]. Of eyes with macular detachment, only approximately 50% end up with 20/40 vision or better. Of those with preoperative visual acuity worse than 20/200, fewer than 15% achieve 20/50 or better [164].

Cystoid macular edema (5–10%) and epiretinal membrane formation (5%) have also been shown to negatively impact the visual outcome of retinal detachment repair [165].

6.7 Infectious and Immune-Mediated Neuropathies

6.7.1 Herpes Zoster Cephalicus (Ramsay Hunt Syndrome)

Hunt first described the syndrome of herpes zoster cephalicus, which is characterized by a viral prodrome followed by severe pain in and around the ear, with vesicles involving the external canal and pinna [166, 167]. Vesiculation may involve the ear, face, neck, tongue, larynx, or buccal mucosa. The distribution of the vesicles depends on which sensory fibers are infected. Any of the nerve branches that communicate with the facial nerve may be involved, including cranial nerves V, VIII, IX, and X and cervical nerves II through IV (Fig. 6.32). In the mildest form, neurologic signs are absent, whereas in severe cases, there may be accompanying sensorineural hearing loss, disturbed vestibular function, and even viral encephalitis. Herpes zoster cephalicus is characterized by vesicles, a high incidence of eighth cranial nerve involvement, postherpetic pain, and a poorer prognosis for recovery of the facial palsy. The presence of hearing loss in a patient with suspected idiopathic facial palsy should strongly suggest varicella zoster virus infection.

The natural history of herpes zoster differs from that of Bell's palsy in several ways, perhaps reflecting the difference in behavior between herpes simplex type 1 and the varicella zoster viruses. Bell's palsy recurs in some 12% of cases, but herpes zoster cephalicus rarely recurs. In addition, the acute phase of the infection, as measured by electrical response and progression of facial weakness, peaks at 5–10 days with Bell's palsy but at 10–14 days with herpes zoster cephalicus. Lastly, 84% of persons suffering from Bell's palsy have a satisfactory recovery of facial

Fig. 6.32 Herpes zoster cephalicus, with Ramsay Hunt syndrome and cutaneous eruption in distribution of second, third, and fourth cervical nerves. (Thank Yuanli Guo for providing this picture.)

function, in contrast to 60% of those with herpes zoster cephalicus.

Treatment of herpes zoster is similar to that of Bell's palsy, but with the addition of therapeutics to control pain and vesicular eruption. Often, narcotics are required. Several studies have supported the efficacy of acyclovir in the treatment of herpes zoster cephalicus [168–170]. One study also suggested that the combination of acyclovir and corticosteroids was superior to a regimen of corticosteroids alone [171].

6.7.2 Polyradiculopathy (Guillain-Barré Syndrome)

Guillain-Barré syndrome (GBS) is an acute inflammatory polyradiculopathy evolving as a paralytic disease. It is of unknown cause but is distinctly immune mediated [172]. Approximately one third of patients may have evidence of *Campylobacter* infection. The characteristic pathologic features of GBS are lymphocytic cellular infiltration of peripheral nerves and destruction of myelin. Therefore, the major complaint is weakness, the severity of which covers a wide spectrum ranging from mild ataxia to total paralysis of any or all motor and cranial nerves. In most instances, symptoms occur first in the legs, but they can begin in the arms, and tendon reflexes are abolished in the affected areas. Facial nerve paralysis occurs in about half the cases and is usually bilateral [173]. Weakness can evolve to total motor paralysis, and when the diaphragm and chest muscles become involved, respiratory embarrassment may lead to death. Abnormal cerebrospinal fluid (CSF) findings are characteristic of this disorder, although in the first few days, the results may be normal. After several days, the protein value begins to rise and may become very high, peaking at about 4–6 weeks after the onset of clinical symptoms. Cells in the CSF are typically absent, but in a small percentage of patients, a mild pleocytosis may exist [173]. In the latter cases, it is important to exclude HIV infection, lymphoma, and vasculitis as possible etiologies. In the variant known as the Miller Fisher syndrome, facial weakness may be present in association with ophthalmoparesis, ataxia, and areflexia. Many of these patients will have GQ1b autoantibodies in their serum. There is evidence that GQ1b-like lipopolysaccharides on *Campylobacter jejuni* may be the immunogens for the synthesis of these antibodies [174].

It has been suggested that Bell's palsy and Guillain-Barré syndrome represent a continuum of a clinical entity ranging from idiopathic unilateral facial paralysis to severe generalized polyneuropathy [175]. Evidence for this theory comes from the work of Abramsky and associates [172]. In patients with Bell's palsy and Guillain-Barré syndrome, a strong similarity in their lymphocyte response to the peripheral nerve basic protein P_1L was observed. Neither disorder showed a lymphocyte response to the other neural antigens (P_2, BE, AChR), which are commonly used to study experimental autoimmune neurologic diseases. In addition, a control group of 26 patients with a wide spectrum of neurologic disorders showed no response to the neural antigens. In our experience, the prognosis for spontaneous facial nerve recovery in Guillain-Barré syndrome is the same as for idiopathic palsy.

6.7.3 Infectious Mononucleosis

Infectious mononucleosis (IM) is characterized by fluctuating fever, sore throat, and lymphadenopathy. Uncommonly, unilateral, recurrent, and simultaneous bilateral facial paralysis has been caused by this disorder. The syndrome of infectious mononucleosis caused by Epstein-Barr virus has a classical presentation and can often be diagnosed on clinical grounds. The prodrome lasts from 3 to 5 days and consists of headache, malaise, myalgia, and fatigue. Sore throat occurs in the first week and is the most common feature of IM. A grayish-white exudative tonsillitis is practically pathognomonic, persists for 7–10 days, and is present in about 50% of cases. Palatine petechiae located near the border of the hard and soft palates are observed in about one third of patients toward the end of the first week of illness. Lymph node enlargement is a hallmark of IM. The onset is gradual, and anterior and posterior cervical lymph node chains are the most commonly involved. IM resembles a number of febrile disorders characterized by fever, sore throat, adenopathy, and lymphocytosis. It may be difficult to distinguish from the early stages of other forms of febrile exudative pharyngotonsillitis, such as streptococcal infections and exudative tonsillitis of viral etiology. The differentiation depends on the results of throat cultures as well as on hematologic and serologic features characteristic of IM. An absolute increase in lymphocytes and monocytes exceeding 50% or more and 10% atypical lymphocytes in the peripheral blood suggest IM. Positive results of a monospot serologic test, a rising titer for heterophil antibodies, and the development of persistent antibody against Epstein-Barr virus confirm the diagnosis.

6.7.4 Lyme Disease

Lyme disease may cause unilateral or bilateral facial paralysis (Fig. 6.33) [176]. This disease is characterized by erythema chronicum migrans, tick-borne meningopolyneuritis, myocardial conduction abnormalities, and Lyme arthritis. The disorder was first recognized in 1975 by close geographic clustering of children with arthritis in the small community of Lyme, Connecticut. The spirochete *B. burgdorferi* is transmitted by an arthropod vector (the deer tick, *Ixodes dammini*). The skin lesion begins as a red macule or papule and expands to form a large red ring with partial central clearing. The lesion typically lasts about 3 weeks or longer (Fig. 6.34). Associated symptoms include malaise, fatigue, chills, fever, headache, myalgias, nausea, vomiting, and sore throat. Some patients develop a spectrum of neurologic symptoms and a clinical picture suggesting collagenosis, syphilis, or multiple sclerosis.

Fig. 6.33 Axial T1-weighted, gadolinium-enhanced MRI showing bilateral proximal facial nerve enhancement (arrows) in patient with Lyme disease and facial diplegia

Cranial neuropathies occur frequently in Lyme disease; facial nerve palsy is the most common of these. Unilateral or bilateral facial nerve palsies occurred in 11% of patients with Lyme disease in one series [176]. In the United States, facial palsy is observed in half the patients with Lyme meningitis. The prognosis for facial nerve recovery with or without therapy is excellent, with the majority of patients achieving satisfactory facial function. Despite the frequent spontaneous resolution of the facial paresis, therapy should be administered to prevent the late neuro-

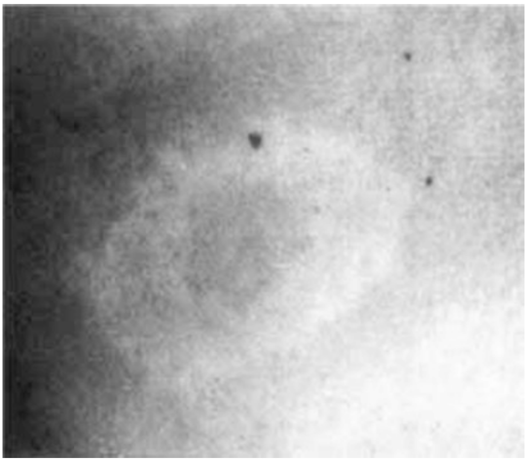


Fig. 6.34 Cutaneous lesion, erythema chronicum migrans, and tick-borne Lyme disease (MacDonald AB: Lyme disease: A neuro-ophthalmologic view. J Clin Neuro-Ophthalmol 7:187, 1987)

logic and arthritic complications that can occur. Interestingly, facial nerve paralysis occurs with or without CSF pleocytosis. Distinguishing Lyme-associated facial palsy from idiopathic (Bell's) palsy is essential. Lyme disease is suggested when there is coexisting multi-organ involvement such as cardiac disease or arthritis. Fever, enlarged lymph nodes, pharyngalgia, and headache are more common with Lyme disease than with Bell's palsy [177]. Nontender swelling and erythema of the face before the onset of the facial palsy may also be a distinguishing feature of Lyme disease [178].

Serologic titers using the enzyme-linked immunosorbent assay (ELISA) and Western blot techniques may help confirm the diagnosis of Lyme disease. However, both false-positive and false-negative Lyme titers are often observed [179]. Because the ELISA and Western blot techniques are not standardized, the reliability of these tests varies widely. In one study, 9 of 40 patients with Lyme disease showed reactivity to the fluorescent treponemal antibody absorption (FTA-ABS) test for syphilis at a 1:5 dilution [180], but in these patients, the Venereal Disease Research Laboratory (VDRL), rapid plasma reagin (RPR), and microhemagglutination assay for *Treponema pallidum* (MHATP) tests were negative. Successful treatment of early Lyme disease has been achieved with either doxycycline or penicillin. When the facial palsy is associated with meningeal inflammation, a 2- to 4-week course of intravenous ceftriaxone is recommended.

6.7.5 Ear Infections

Despite the frequency of acute otitis media, particularly in children, associated facial paralysis is quite uncommon. In these cases, the facial nerve is most vulnerable because it traverses the tympanic portion of the fallopian canal. The infectious process may track along the chorda tympani nerve, the stapedius nerve, or the posterior tympanic artery to reach the facial nerve within the fallopian canal. The presence of a congenitally narrow fallopian canal is an important risk factor for the development of a facial palsy in acute otitis media [181]. Delayed facial palsy occurring several weeks after a bout of acute otitis media suggests a secondary mastoiditis. A spontaneous and satisfactory recovery is the usual course after treatment with appropriate antibiotics and myringotomy. Surgical therapy is indicated if the infection does not respond to these measures.

Chronic suppurative infection of the middle ear has a different natural history and does call for immediate surgical intervention when associated with a peripheral facial paralysis. Often the pathologic process involves compression of an exposed nerve by cholesteatoma or chronically infected granulation tissue [182]. Abscess and osteitis are not unusual findings at the time of surgery.

In cases of complicated otitis media, localized inflammation of the petrous apex may occur, resulting in the so-called Gradenigo's syndrome [183]. This entity is characterized by facial pain associated with trigeminal, abducens, and facial nerve palsies. Neuroradiologic imaging should be performed to exclude the presence of an extradural abscess or mass lesions that might mimic Gradenigo's syndrome, such as invasive nasopharyngeal carcinoma. Treatment consists of appropriate antibiotic coverage and possible surgical debridement of the petrous bone.

A closely related disorder is the malignant external otitis syndrome. This infectious disorder is usually seen in elderly patients with diabetes and begins in the external auditory canal. The offending organism is *Pseudomonas aeruginosa.* The facial nerve may be involved at the level of the stylomastoid foramen by an associated necrotizing osteomyelitis, which may spread to involve the occipital bone, clivus, and contralateral petrous pyramid. Other complications include venous dural thromboses, meningitis, and brain abscess. Treatment should consist of broad-spectrum antibiotics effective against all strains of *P. aeruginosa.* Facial nerve paralysis is reversible until the nerve itself becomes necrotic [184, 185].

6.7.6 Other Infections and Postimmunization

Facial nerve paresis has been observed in a variety of other infectious processes, including chicken pox [186], mumps [186], influenza [187], brain stem encephalitis [187], polio [188], enterovirus [189], leprosy [190], tuberculosis [191], mucormycosis [192, 193], syphilis [194], tetanus [195], diphtheria [196], *Bartonella henselae* [197], and human monocytic ehrlichiosis [198]. Facial paresis has also occurred after vaccination [199–201] and after the administration of tetanus antiserum [202]. Unilateral or bilateral facial palsy has been observed in HIV infection. The facial palsy associated with early HIV may spontaneously resolve and has been documented to occur at the time of HIV seroconversion [203]. In contrast, the appearance of a facial palsy in the advanced stages of HIV infection should prompt a search for other etiologies, such as meningeal lymphoma, herpes zoster, and cryptococcal meningitis.

6.8 Infective Neuropathies

Of those optic neuritides in which infectious agents are more readily apparent, the impact of human immunodeficiency virus (HIV) infection and acquired immune deficiency syndrome (AIDS) has most palpably altered the modern etiologic spectrum. HIV-associated optic nerve disease may be related to tumoral compression, infiltrations such as lymphoma, vasculitides, inflammations, and especially secondary infections. Opportunistic infectious agents regularly invade the retina, optic nerve, meninges, and brain, and coexisting multiple infections further confound diagnosis and management. Neurologic symptoms are said to occur in 40% of cases, CNS pathologic findings in 70% to 80%, ocular manifestations in 50% to 70%, and neuro-ophthalmologic signs in at least 3% to 8% [204, 205]. Optic nerve complications of immunodeficiency are included in Table 6.11.

Table 6.11 Optic neuropathies in immunodeficiency

Papilledema (raised cerebrospinal fluid pressure)
Cryptococcal meningitis
Toxoplasmosis
Lymphoma
Optic neuritis
Cryptococcosis
Syphilis (perineuritis form)
Cytomegalovirus
Pneumocystis carinii
Human immunodeficiency virus?
Histoplasmosis
Varicella

AIDS-related optic neuropathies generally reflect direct infestations of viral, spirochetal, or fungal organisms, but grossly diminished axonal counts may indicate a primary AIDS optic neuropathy [206]. Otherwise, cytomegalovirus retinitis with spread to the nerve, or as an initial papillitis, is associated with poor visual outcome even with therapy [207]. Likewise, cryptococcosis (Fig. 6.35) may be associated with chronic optic meningitis, with insidious or rapid vision loss related to fulminant nerve necrosis [208]. Optic nerve sheath decompression for raised CSF pressure in cryptococcal meningitis has been reported to improve function [209]. Other infectious agents include *Toxoplasma gondii* [210], varicella zoster [211, 212], and *Histoplasma capsulatum* [213].

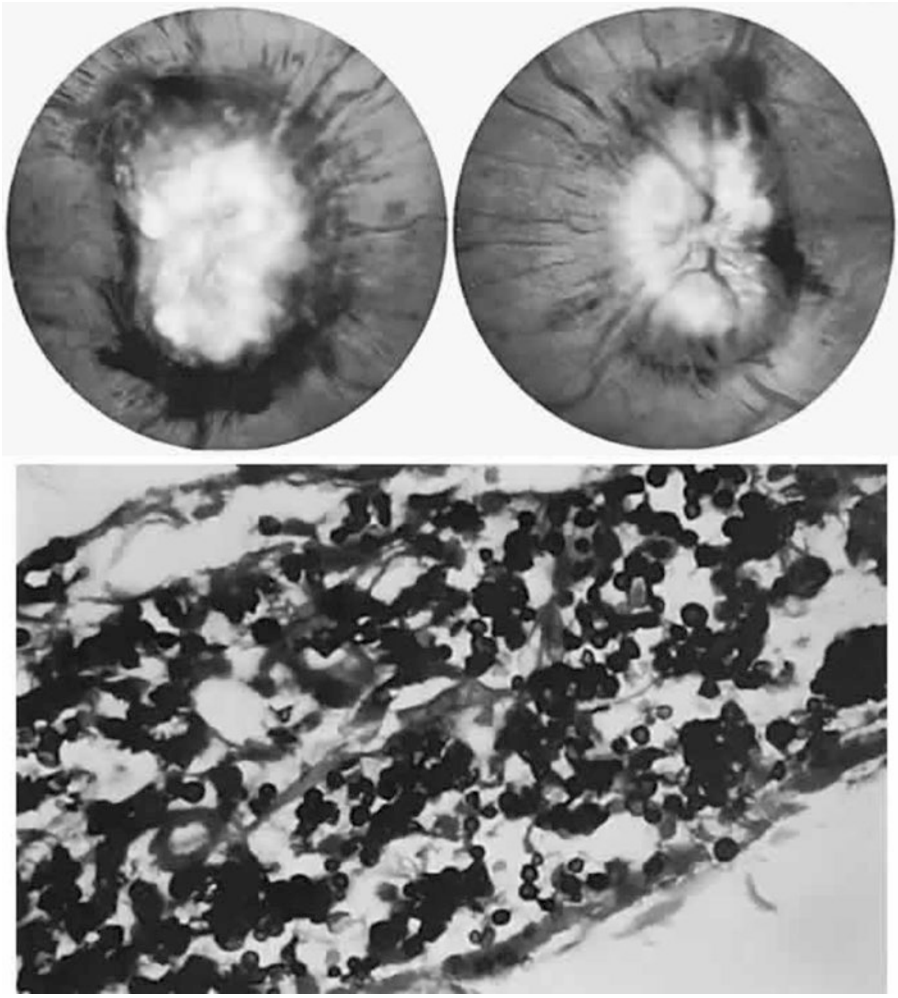


Fig. 6.35 Cryptococcosis with severe hemorrhagic disc swelling. Visual function of hand movement in each eye. At autopsy, organisms were found within the meninges and substance of the optic nerve

The role of HIV itself as an etiologic agent in optic nerve disease is imprecise, but the virus has been isolated from all ocular tissues; it is neurotropic and is implicated in cases of meningitis (including with *Cryptococcus*), encephalitis, and peripheral neuropathies [214]. Indeed, HIV-seropositive patients are reported with recoverable bilateral optic neuropathies without other infectious or neoplastic processes, suggesting a primary role of HIV infection [215]. Berger and associates [214] described a neurologic disease clinically indistinguishable from MS, including mostly bilateral optic neuritis, occurring with HIV; indeed, histopathologic features of the CNS were consistent with MS.

By 1990, the incidence of primary and secondary syphilis in the United States increased 34% to 18.7/100,000 persons, and serologic testing is indicated in many cases of optic neuropathy without other clearly discernable causes but especially in patients with, or at risk for, AIDS. Coinfection alters the natural history and increases the propensity for a more aggressive course and rapidly evolving neurosyphilis. Moreover, even in biopsy-confirmed syphilis, treponemal and nontreponemal tests may be neg-

ative in HIV infection [204]. Corticosteroids, so frequently used in optic neuritis, are contraindicated until infectious causes are ruled out, including CSF assessment, especially when HIV is suspected. Empiric penicillin treatment for neurosyphilis may be considered [215]. Modern laboratory tests include the fluorescent treponemal antibody absorption (FTA-ABS) test and microhemagglutination assay.

Syphilitic neuroretinitis, papillitis, and "perineuritis" are clinical manifestations of secondary stage and neurorecurrence, whereas slowly progressive atrophy evolves in the tertiary stage; simple papilledema of raised pressure may herald meningoencephalitis [216]. Uncomplicated "retrobulbar" neuritis, so common otherwise, must be extremely rare in syphilis, although Zambrano [217] reported bilateral overnight blindness in association with AIDS. Optic "perineuritis" purportedly inflames primarily the optic meninges, with relative sparing of the central core of the nerve and preservation of central field function, including acuity; disc swelling is characteristic, but papilledema of increased pressure and meningitis are ruled out by lumbar puncture. Color vision and evoked potentials may be normal [218]. Late "descending" optic atrophy is a sign of tertiary neurosyphilis, classically seen in taboparesis.

Arruga and colleagues [219] reviewed neuroretinitis in acquired, secondary syphilis, with funduscopically evident clouding of the central retina, vasculitis, hemorrhages, pigment epithelial disarray, and disc swelling; most cases are bilateral, and vitreous cellular debris is present.

Lyme borreliosis must be an uncommon cause of optic neuropathies or of any other ocular manifestations, according to authoritative reviews [220] of neurologic manifestations of the disease. In the early disease, a nonspecific follicular conjunctivitis occurs in about 10% of patients, and flu-like symptoms are common along with the typical *erythema migrans* rash, itself noted in only 60% to 80% of cases. Uveitis is extremely rare, as is neuroretinitis. Schmutzhard and associates [221] included two young women with "optic neuritis," and Pachner and Steere [222] cited no optic nerve involvement among 38 cases of Lyme meningitis. The case report of Wu and coworkers [223] of "optic disc edema" seemingly occurred in the setting of a 7-year-old boy with stiff neck and CSF pleocytosis. Strominger and colleagues [224] reported worsening of Lyme neuroborreliosis, including optic neuritis, following ceftriaxone therapy. In the *early disseminated phase*, aseptic meningitis, cranial neuropathies (facial palsy being the most common), and radiculoneuritis occur. Indirect immunofluorescence antibody (IFA) and enzyme-linked immunosorbent assays (ELISA) are used to detect antibodies, but even for patients with the pathognomonic cutaneous manifestation of erythema migrans, in a Connecticut study, the overall sensitivity of serology was 30% to 45% by IFA and 24% to 32% for ELISA [225]. At present, seropositivity alone does not distinguish between past exposure and active infection, and false-positive results are common. Polymerase chain reaction techniques are currently being evaluated [221]. In the early stages, doxycycline or penicillins are used, and ceftriaxone is used for neurologic or ophthalmic disease [221].

Cat-scratch disease is an infection caused by *Bartonella* (*Rochalimaea*) *henselae* and *R. quintana*, gram-negative bacilli implicated in subacute regional lymphadenitis, conjunctivitis (at times with preauricular adenopathy), intermediate uveitis, retinal vasculitis, serous retinal detachment (see also Part I of this chapter), papillitis with retinal exudates, and aseptic meningitis [226, 227]. Disease evolves days to weeks after cat scratch or bite, and it is thought that almost 50% of domestic cats, and their fleas, are the persistent reservoir of these organisms. Visual acuity is variable, and papillitis may be bilateral. IFA of serum is positive in the majority of patients, but serologic assays are also positive in some 3% of the healthy population. Although cat-scratch disease is considered a self-limited and relatively benign infectious disorder, and no optimal therapy is yet defined, various antibiotics are usually administered to maximize visual outcome [227]. Reed and colleagues [76] suggested the use of doxycycline and rifampin.

Toxocara canis [228] is also documented to cause inflammatory papillitis with vitreous cel-

lular reaction. *Toxoplasma gondii* (the agent of toxoplasmosis), a relatively frequent cause of posterior uveitis in the United States, with characteristic pigmented chorioretinal scars, is an uncommon but eradicable agent that can produce neuroretinitis characterized by retinal edema with macular star exudates. Serologic tests include IFA titers and ELISA, and sulfamethoxazole, sulfadiazine, or clindamycin therapy is indicated, usually coupled with corticosteroids [229]. Familial Mediterranean fever (recurrent polyserositis), an autosomal recessive disorder, is reported to produce uveitis, retinal detachment, or optic neuritis [230].

6.9 Superior Orbital Fissure Syndrome (SOFS)

This fissure lies at the back of the orbit between the lesser and great wing of the sphenoid. It curves downwards and medially widens at the orbital apex containing the superior ophthalmic vein, ophthalmic division of the trigeminal nerve and branches (lacrimal, frontal, supraorbital, supratrochlear, and nasociliary), and the nerves to the extraocular muscles.

The syndrome is characterized by retro-orbital paralysis of extraocular muscles, impairment of the branches of the first division of the trigeminal nerve, and frequently extension to involve the optic nerve. Examination shows ophthalmoplegia, ptosis, decreased corneal sensation, and occasionally visual loss caused by mechanical optic nerve compression. The presence of proptosis, with swelling of eyelids and chemosis (swelling of ocular surface membranes), indicates significant mass extension within the orbit.

Potential causes include traumatic craniomaxillofacial injuries, tumors of the orbit (lymphoma or rhabdomyosarcoma) and adjacent structures, infection, inflammatory disorders, and vasculitic and ischemic diseases. Orbital inflammation may be isolated (nonspecific orbital inflammation) or associated with systemic inflammation such as Wegener's granulomatosis, polyarteritis nodosa, sarcoidosis, or, rarely, temporal arteritis. Fungal infection of the orbit is an important though rare cause of an orbital apex syndrome and is usually secondary to sinus involvement.

The cavernous sinus extends posteriorly from the superior orbital fissure to the dorsum sellae. The fissure and the anterior cavernous sinus contain the same structures, and determining which is involved in the absence of orbital mass signs is dependent on imaging.

Dislocated bony fragments or comminuted fractures in the region of the superior orbital fissure or of the lesser wing of the sphenoid cause direct nerve lesions. If all cerebral nerves entering at this point are involved, a complete superior orbital fissure syndrome results.

6.9.1 The Complete SOFS

The complete SOFS results from a paresis of the cerebral nerves III, IV, and VI. Clinically there is an ophthalmoplegia with ptosis and an exophthalmus due to disruption of the venous drainage. In addition, a mydriasis and an accommodation paralysis (cycloplegia) occur due to loss of the parasympathetic innervation. If the abducent nerve is still intact, abduction of the eyeball may still be possible [231].

Anesthesia in the areas of sensory innervation is inevitable if the sensory branches of the ophthalmic nerve are involved. A severe retro-orbital pain sometimes occurs in combination with a supraorbital neurogenic pain as a result of the complex damage that has occurred [232].

As a consequence of fragment dislocation, decompression of the orbital fissure via the frontotemporal access is necessary (Fig. 6.36) [233].

6.9.1.1 Symptoms

- Complete ophthalmoplegia (nerves III, IV, VI)
- Ptosis
- Mydriasis – accommodation paralysis (cycloplegia)
- Loss of sensibility (ophthalmic, nasociliary nerve)
- Retro-orbital pain
- Possible abduction of the eyeball

Fig. 6.36 Complete right upper orbital fissure syndrome with palsy of cranial nerves III, IV, and VI following lateral midface fracture and fracture of the greater wing of the sphenoid (6 weeks post surgery)

Fig. 6.37 Incomplete left superior orbital fissure syndrome with palsy of the oculomotor nerve. Mydriasis, partial ophthalmoplegia, ptosis, and exophthalmia following fractures of the zygoma and sphenoid wing

6.9.2 Incomplete SOFS

Due to the fact that three oculomotor nerves enter through the superior orbital fissure, injuries to the individual branches may lead to a selective paresis, so developing the image of a partial SOFS. Frequent injuries occur in the caudal region of the superior orbital fissure. The clinical loss is usually limited to the restriction of the vertical motility of the eyeball due to partial damage of the nerves III and IV, a ptosis, an abnormal pupil reaction, and anesthesia in the innervation area of the nasociliary nerve [232]. Isolated damage to the parasympathetic element of the third cerebral nerve leads to a temporary mydriasis; this occurs relatively often in lateral midface fractures (Fig. 6.37).

6.9.2.1 Symptoms

- Partial ophthalmoplegia (nerves III and/or IV)
- Ptosis
- Mydriasis
- Accommodation paralysis (cycloplegia)

6.10 Orbital Apex Syndrome (OAS)

If retro-orbital fractures not only affect the superior orbital fissure but lead to an immediate lesion of the optic nerve, an OAS develops [234, 235]. The orbital apex syndrome includes all symptoms of superior orbital fissure syndrome plus optic nerve involvement, leading to changes in visual acuity.

In this case, a high-grade loss of visual acuity or an amaurotic complete iridoplegia occurs. In addition, there is paresis of the three cranial nerves III, IV, and VI (Fig. 6.38) [232, 236–238].

6.10.1 Symptoms

- Loss of function of cranial nerves III, IV, and VI
- Damage of the optic nerve (N. II) with loss of visual acuity

Fig. 6.38 Orbital apex syndrome with internal ophthalmoplegia and amaurosis and complete iridoplegia following zygomaticoorbital fracture on the right

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7 Acute Pain in the Eye

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Abstract

A painful eye is not normal, is commonly associated with various sensations, and the accompanying symptoms may be indicative of an ocular emergency. Among those, accompanying vision problems and/or redness of the eyeball require special attention to prevent blindness. A differential diagnosis should be made at presentation by careful ophthalmic examination. Proper management should be instituted in a timely manner to obtain maximum benefit in a patient presenting with acute pain in the eye. This chapter aims to provide an overview on current approaches in an eye with acute pain and glaucoma, scleritis, uveitis, and corneal problems.

Keywords

Acute pain · Glaucoma · Scleritis · Uveitis · Corneal abnormalities

7.1 Introduction

Similar to acute vision loss, red eye, and photophobia, acute pain in the eye is one of the typical symptoms of an ocular emergency. Although acute eye pain may result from numerous pathologies, an appropriate history will often help the ophthalmologist disclose the underlying disease.

Ocular pathologies that affect the ocular somatosensory pathway may cause ocular pain. It is well-known that the cornea has one of the most sensitive nociceptors in the body. It is estimated that 7000 nociceptors per mm^2 are available in the human corneal epithelium [1], which is 300–600 times greater than the density of nociceptors in the dermis [1, 2]. These nociceptors are placed superficially between the epithelial cells [1] and transmit the pain sensation to the ophthalmic branch (majority) and maxillary branch of the trigeminal nerve [3].

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First of all, a detailed anamnesis should be obtained from patients admitted with acute ocular pain. A query of previous ocular diseases (glaucoma, diabetic retinopathy, retinal vascular occlusion), systemic diseases (diabetes mellitus, hypertension, sickle cell anemia), medications (anti-glaucomatous, blood thinners), ocular trauma, and ocular surgery can be very important both diagnostically and therapeutically.

Factors that aggravate the ocular pain should also be questioned. For example, optic neuritis is characterized by ocular pain that is usually exacerbated by eye movements, whereas eyelid movements often increase a foreign body-welded ocular pain.

7.2 Ophthalmic Examination

External inspection of ocular and periocular tissues should be performed under both daylight and with a bright light source in order to detect a clue for ocular pain. Uveitis-induced ciliary injection and episcleritis-induced red eye cases can be evaluated under daylight more accurately. Meanwhile, pupils must be evaluated in terms of their shape, size, and light response. Evaluation of the eye movements and the visual field with confrontation should be performed, especially in patients with suspected optic neuritis.

Best corrected visual acuity (BCVA) gives information about the current status and the future prognosis of patient. It should be kept in mind that recording the BCVA is also crucial in order to avoid medicolegal problems. Afterward, detailed slit-lamp examination of both eyes, posterior segment examination (if possible), and gonioscopic examinations must be performed. Lastly, imaging techniques as ultrasonography, ultrasonographic biomicroscopy, X-ray, computed tomography, and magnetic resonance imaging may be requested if necessary.

We will focus in this chapter on the most common causes of acute eye pain.

7.3 Acute Elevation of Intra ocular Pressure

Regardless of the reason, acute IOP elevation causes the following damages to ocular tissues: corneal endothelial cell loss, ischemic iris damage, anterior lens epithelium infarct (glaukomflecken), trabecular meshwork (TM) damage, and optic nerve head damage [4, 5]. van der Heijden et al. [6] also demonstrated that both acute and chronic IOP elevations affect the scotopic and photopic contrast sensitivity and cause retinal ganglion cell loss in mice.

7.3.1 Angle-Closure Glaucoma

Definition

The European Glaucoma Society described the term of “angle closure” as the occlusion of the TM by iridotrabecular contact (ITC) [4], which requires a gonioscopic examination for diagnosis and grading [7]. Angle closure results in acute IOP elevation due to closure of the aqueous outflow channels. While primary angle closure (PAC) refers to closure of the angle by the peripheral iris in an anatomically predisposed eye, secondary angle closure is defined when it occurs secondary to other ocular disorders. It is estimated that PAC glaucoma (PACG) constitutes approximately one quarter of all glaucoma cases [8]. However, PACG is responsible for 50% of all glaucoma-related blindness worldwide, because it is associated with faster progression compared to open-angle glaucoma [4, 5, 7, 8]. If treated properly, this faster progression and late complications can be prevented. Therefore, early diagnosis and treatment of PAC is very important. Gonioscopic examination of all patients with glaucoma at the initial visit and in case of angle-closure suspicion is the essential step for early diagnosis.

Classification [4, 5, 9]

It can be classified into three groups according to spectrum of angle closure:

(a) Primary angle-closure suspect (PACS): Presence of ITC in two or more quadrants without IOP increase, peripheral anterior synechiae (PAS), and evidence of glaucomatous optic neuropathy (GON).
(b) Primary angle-closure (PAC): Presence of ITC with PAS and/or increased IOP without evidence of GON. PAS and increased IOP should not be due to another systemic or ocular disorder.
(c) Primary angle-closure glaucoma (PACG): Presence of ITC with evidence of GON. PAS and/or increased IOP may not exist at initial examination.

Risk Factors

There are many risk factors that facilitate the development of the PAC.

Age: The prevalence of PAC increases with older age [4, 5, 7, 8, 10]. The mean age of patients with PACG at presentation is 60 years [5]. Day et al. [10] declared that the age-specific prevalence values of PACG in European-derived populations are as follows: 0.02% for those 40–49 years, 0.60% for those 50–59 years, 0.20% for those 60–69 years, and 0.94% for those 70 years and older.

Gender: Women are approximately 3.0–3.25 times more prone than men in terms of development of PACG [7, 8, 10, 11], due to shallower anterior chamber and narrower iridocorneal angle compared to men in all age groups [11].

Race: PACG is most frequently seen in the Asian-descent people, and the highest prevalence is in China all over the world [8, 12]. PACG accounts for approximately 90% of bilateral glaucoma blindness cases in China [12].

Family history: Studies show that the risk of PACG is increased in patients with one family member affected by PACG [5, 13, 14].

Refraction: Small, hypermetropic eyes with shorter anterior chamber and axial length are more prone for developing PACG [5, 14]. Furthermore, in an ultrasound biomicroscopic and conventional ultrasonographic study, Marchini et al. [15] identified that the lens is more anteriorly located due to forward rotation of the ciliary processes in PACG and consequentially the crowded anterior segment is a risk factor for PACG. Angle crowding, which refers to angle closure in response to the compression of the iris between the TM and angle structures, is considered as another risk factor for PACG. Nanophthalmos and plateau iris configuration set examples of these two predisposing situations for PAC [16, 17].

Clinical Presentation and Signs

Most angle-closure incidents happen asymptomatically [4, 5, 7]. Only prolonged and remarkable angle closures lead to IOP elevation, and the patients may be admitted to hospital with complaints of eye pain, redness, blurred vision, haloes around lights, and headache. There may be some precipitating factors such as reading, watching cinema, emotional stress, parasympathetic antagonist, or sympathetic agonist drugs. However, the diagnosis can be missed, as these symptoms are not specific for angle closure.

During ophthalmic examination of patients with acute angle closure, decreased BCVA (6/60 – hand motion), mid-dilated and unreactive pupil, ciliary injection, narrow anterior chamber, aqueous flare, corneal epithelial edema, and very high IOP (>50 mmHg) can be determined (Fig. 7.1). Depending on the reason of the angle closure, some additional pathological signs can also be seen (Fig. 7.1). Examination of the fellow

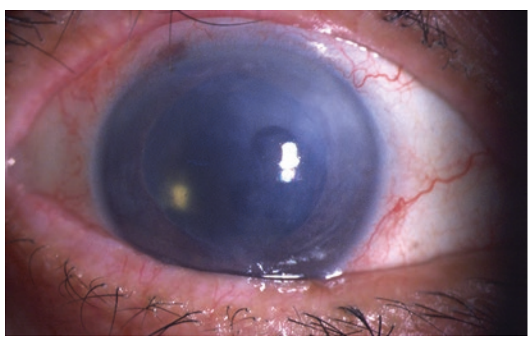

Fig. 7.1 The slit-lamp photo demonstrates a mild ciliary injection, corneal edema, and a dilated and nonreactive pupil in a patient with neovascular (secondary angle-closure) glaucoma. Also note the rubeosis iridis, which may be overlooked in this case due to corneal edema

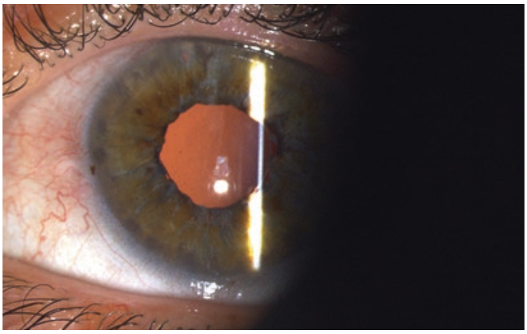

Fig. 7.2 The contralateral eye of a patient presenting with acute angle-closure glaucoma reveals a small but patent iridotomy at the 11 o'clock position. The patient has also been treated with lens surgery. In addition, the pupil appears irregular due to iris atrophy, which indicates previous attacks of angle closure

eye with occludable iridocorneal angle or iridotomy will assist in the diagnosis (Fig. 7.2).

Management

The principle of the management of the acute angle closure is to control elevated IOP and open the angle. Determining the mechanism of angle closure is important in order to treat the patient properly and to manage the underlying disorder. Pupillary block (i) is the most commonly seen mechanism (75% of patients with PAC). Other mechanisms such as (ii) anomalies of the iris and/or ciliary body (plateau iris), (iii) anomalies of the lens (diabetic, traumatic, or subluxated cataract), and (iv) anomalies posterior to the lens (aqueous misdirection) are seen rarely.

- **Medical Treatment**
- Medical treatment constitutes the core of management to lower IOP, improves the patient's symptoms, and provides the proper circumstances for laser treatments.
  – Patient should be in a supine position in order to shift the lens posteriorly.
  – Hyperosmotics (20% mannitol, intravenous in 30 min, and glycerol, orally) are administered in order to decrease the volume of vitreous and posterior chamber by decreasing the blood osmolality and increasing the blood-aqueous osmotic gradient.
  – Carbonic anhydrase inhibitors (acetazolamide 500 mg, intravenous if IOP > 50 mmHg and orally if IOP < 50 mmHg) are given to suppress aqueous humor production.
  – Topical aqueous suppressants such as β-blockers, α-agonists, carbonic anhydrase inhibitors, and pilocarpine can be used in order to lower IOP level. The use of topical prostaglandin analogues in PACG is controversial. Although they can be effective, there is controversy in terms of increasing ocular inflammation.
  – Miotics (2–4% pilocarpine one drop, repeated after half an hour) are administered in order to change the configuration of the trabecular meshwork and to improve aqueous outflow by contracting the ciliary and pupillary sphincter muscles (miosis). Pilocarpine may be ineffective in the conditions of pupil paralysis and ischemic iris atrophy due to high IOP.
  – Topical steroids (1% prednisolone or 0.1 dexamethasone, every 5 min for three times and then four to six times daily) should be given to reduce inflammation.
  – Analgesics and antiemetics may be given if required.
- **Laser Treatment**

The aim of laser treatment is to prevent the recurrence of angle-closure episodes. It can be performed immediately after resolution of corneal edema and attainment of normal IOP by medical treatment. Prophylactic laser treatment to the fellow eye is usually recommended, if it also has a narrow angle [18].

– Nd:YAG laser iridotomy: Although, Nd:YAG laser is the more preferred option currently, argon laser treatment can also be performed in patients with dark and densely pigmented irides. Laser peripheral iridotomy equalizes the pressure of anterior and posterior chambers by

creating a permanent opening, and the iris flattens and moves posteriorly away from the angle. However, iridotomy is ineffective in patients without pupillary block [18, 19]. Argon laser peripheral iridoplasty (ALPI) may provide opening of the angle in these cases.

– Argon laser peripheral iridoplasty: ALPI is performed to widen the anterior chamber angle. It provides movement of the iris away from the TM and opening of the angle as the small burns on the surface of the peripheral iris contract the iris stroma. It is an effective treatment modality for angle closure due to mechanisms other than pupillary block, such as plateau iris syndrome [20, 21].

Laser Iridotomy Application

- Instill pilocarpine drops before the procedure to reduce the pupil size and to reduce the thickness of iris.
- Instill a drop of apraclonidine or brimonidine 30 min before the procedure to prevent early IOP rise.
- Insert an iridotomy lens (Abraham or Wise) on the cornea, after using topical anesthetic drops.
- Target an iris crypt or a thin area of the iris.
- Preferably, select the superior quadrant and peripheral iris to minimize the risk of glare (or monocular diplopia) and lens damage, respectively. However, the 12 o'clock position is not recommended due to the risk of closure of the iridotomy by any bleeding.
- Set the laser power to 2–5 millijoules depending on the iris features of patient.
- Focus the beam precisely and fire the laser. 5–10 shots are usually required for creating an adequate iridotomy. Avoid opening a very small or a very big iridotomy.
- A gush of aqueous fluid or iris pigment indicates a successful iridotomy procedure.
- Instill a drop of apraclonidine or brimonidine again.
- Continue to use antiglaucoma drugs and steroids.

Possible Complications of Procedure

- Bleeding: It is the most common complication (50%). It usually stops spontaneously in several seconds. If it persists, it can be ceased by pressing the contact lens.
- IOP elevation: It is usually transient and occurs within one hour of procedure.
- Iritis: It is especially common in darker-pigmented irides. If adequate steroid treatment is not administered, posterior synechiae may develop in cases with severe iritis.
- Corneal burn: If a contact lens is not used or the anterior chamber is extremely shallow, corneal burns may occur. It usually recovers spontaneously.
- Lens opacity: A non-progressive and localized opacity at the laser application site may develop.
- Some rare complications such as corectopia, cystoid macular edema, involuntary retinal injury, and malignant glaucoma may also occur after laser iridotomy.

Argon Laser Peripheral Iridoplasty Application

- Instill a drop of the pilocarpine and apraclonidine or brimonidine.
- Insert an iridotomy lens (Abraham or Wise) or Goldmann three-mirror lens on the cornea, after applying topical anesthetic drops.
- 1–2 burns of argon laser per clock hour (approximately 25 shots) with 500 μm

size, 100–500 mW power, and 0.2–0.5 sec duration are performed to the peripheral iris.

- The aim is to create a slight iris contraction.
- Occurrence of slight iris contraction during the procedure indicates adequate treatment.
- Instill a drop of apraclonidine or brimonidine again.
- Topical steroids hourly for the first day and then four to six times daily.
- Topical antiglaucoma drugs, if required.

Possible Complications of Procedure

- Transient and mild iritis, IOP rise, and accommodation alterations can be seen.

- **Surgical Treatments**
  - Anterior Chamber Paracentesis

It is a controversial procedure. It can be used as an alternative method in acute angle-closure cases. It provides the relief of symptoms and prevents further damage to ocular structures by decreasing the IOP rapidly [22]. However, the IOP lowering effect of this procedure loses its effectiveness in about 1 h [23]. It can also lead to some complications such as iris and lens injuries, excessive shallowing of the anterior chamber, choroidal effusion, and endophthalmitis [23].

– Surgical Iridectomy

It is more and more rarely required in the era of laser iridotomy. It may be used in patients in whom laser treatment fails due to corneal edema.

– Lens Extraction

The lens plays a crucial role in the pathogenesis of angle closure. It is well-known that lens extraction reduces pupillary block and angle crowding and increases the anterior chamber depth [22, 24]. Furthermore, lens extraction may provide a greater reduction in synechial angle closure and greater increase in the anterior chamber depth and angle in patients with PACG compared to trabeculectomy [25]. Surgical lens removal is undisputed in lens-induced angle-closure cases such as phacomorphic glaucoma and lens subluxation glaucoma and in patients with glaucoma coexisting with cataract. However, the conduct of this surgery in patients with acute angle closure without cataract remained controversial until the EAGLE study [26]. The EAGLE study, which was a randomized and controlled trial, enrolled 419 patients with newly diagnosed PAC or PACG. The outcomes of two different treatment modalities were compared as initial treatment: clear lens extraction (208 patients) versus standard care (211 patients) with laser peripheral iridotomy and topical medical treatment. They demonstrated that surgical lens removal had greater efficacy, and it was more cost-effective than standard care treatment [26]. They recommended that this procedure should be considered as an option for first-line treatment in patients with PAC.

– Trabeculectomy

Trabeculectomy, which is considered the gold standard treatment modality for all glaucoma subtypes among many glaucoma specialists, has been performed in patients with medically uncontrolled acute PAC. Although the success rate of trabeculectomy in primary open-angle glaucoma (POAG) is relatively high, it has been found to be unacceptably low in acute PAC cases [27]. It is also associated with high-risk postoperative complications. Furthermore, some authors even do not recommend trabeculectomy as a treatment modality in patients with acute PAC [27]. However, both phacoemulsification and trabeculectomy were found to be effective in lowering IOP levels in medically unresponsive chronic angle-closure glaucoma cases [28].

– Combined Phacotrabeculectomy

If the patient with PACG has a coexisting cataract, combined phacotrabeculectomy may be performed. Wang et al. [29] reported similar levels of IOP reduction and complications after trabeculectomy alone and combined phacotrabeculectomy in PACG patients. In another study, Tham et al. [30] reported that phacoemulsification

resulted in significantly less surgical complications than combined phacotrabeculectomy in chronic angle-closure glaucoma with cataract.

– Other Surgical Treatment Modalities

Shunt implants, goniosynechialysis, and cyclodestructive procedures are among the rarely performed surgical treatment modalities in PAC cases [31–34].

7.3.2 Angle-Recession Glaucoma

Definition

Angle recession or cleavage is one of the secondary causes of open-angle glaucoma. Angle recession, which often develops secondary to blunt ocular trauma, is a disorder of separation of longitudinal and circular muscles of ciliary body [5, 35]. Angle recession occurs as a result of aqueous movement toward the angle due to a sudden IOP elevation [36]. The patients with angle-recession glaucoma usually present with a unilateral IOP elevation months to years following ocular trauma. While the early-onset glaucoma within days to weeks of ocular trauma is usually seen because of other causes such as plugging of TM with red cells or inflammatory cells, anterior lens dislocation, corticosteroid usage, and ruptured lens capsule; late-onset glaucoma, which by definition develops 6 months after trauma, is most commonly associated with angle recession [37–40].

Risk Factors

It is well-known that there is a high correlation between the risk of development of glaucoma and the presence of angle recession and also its degree after an ocular trauma [41]. Ng et al. [37] investigated the incidence of angle recession and glaucoma in 97 patients who had traumatic hyphema. They determined that all of the late-onset glaucoma patients had angle recession. They identified that the development of glaucoma was related to presence of angle recession >180°, whereas other factors such as the initial BCVA, the presence of lens injury and iridodialysis, the amount of hyphema, and the demographic features of the patient were not associated with the development of glaucoma.

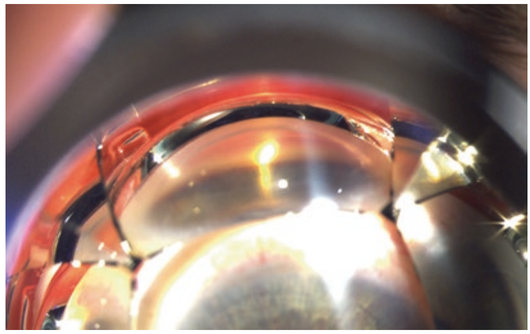

Fig. 7.3 Gonioscopic examination reveals a widened angle together with a posterior shift of the iris

Clinical Presentation and Signs

Presentation of angle-recession glaucoma resembles POAG. It can be differentiated by the presence of a history or findings of ocular trauma and presence of the classic gonioscopic findings. In gonioscopic examination (Fig. 7.3), irregular widening of the ciliary body, white glistening scleral spur, peripheral anterior synechia at the border of recession, and depression of the TM are seen initially, whereas hyperpigmentation and fibrosis are seen in long-standing cases [5, 35].

Most of the angle-recession glaucoma patients are relatively young males because there is a male predominance of ocular trauma cases in all age periods, even in pediatric ages [42]. The most commonly seen anterior segment complication of blunt eye injuries is angle recession [43]. Therefore, all patients with a history of ocular trauma should be examined gonioscopically for angle recession, especially patients who developed microhyphema or gross hyphema [37]. However this examination is not recommended in the acute period of ocular trauma. The patients should also be followed continually because angle-recession glaucoma may develop at any time after ocular trauma. The glaucoma incidence has been identified as 2–10% in patients with angle recession within 10 years [44]. Ng et al. [37] found the interval time between the onset of glaucoma and the time of ocular trauma ranged between 10 and 79 months (mean, 47.6 ± 28 months) in their retrospective study with a 10-year follow-up period. Pilger and Khwarg [45] reported two cases with angle-recession glaucoma which developed 19 and

23 years after ocular trauma. Therefore, a history of ocular trauma should absolutely be questioned in unilateral open-angle glaucoma cases. However, both the ophthalmologists and patients frequently overlook this issue.

Management

Management of posttraumatic angle-recession glaucoma is challenging [5, 35–41, 44–49]. While medical treatment is not generally satisfactory, laser trabeculoplasty is also often ineffective. Pilocarpine usage is controversial. It may cause a paradoxical IOP elevation by decreasing the uveoscleral outflow [35, 50]. Mermoud et al. [41] compared the success rates of three different surgical procedures for unresponsive angle-recession glaucoma. They demonstrated that trabeculectomy with antimetabolites is more effective than single-plate Molteno implantation or trabeculectomy alone. They found the success rate of trabeculectomy without antimetabolite use as 62% after 2 years of follow-up, 42% after 4 years, and 10% after 6 years. They thought that the poor long-term success rate may be related to the demographic features of their series (young age and black race) or increased tendency for fibroblast proliferation related to ocular trauma. The same study group also identified that the angle recession was a risk factor for failure of trabeculectomy [46]. They determined that the mean duration for bleb failure was 3.1 ± 1.2 months in 35 patients with angle-recession glaucoma and 9.4 ± 5.0 months in 35 patients with POAG. Therefore, patients with angle-recession glaucoma should be considered intractable cases for trabeculectomy, and adjunctive antimetabolite use appears to be almost mandatory. In case of failure after filtering surgery, shunt surgery can be performed [48, 49].

7.3.3 Pigmentary Glaucoma

Definition

Pigment dispersion syndrome (PDS), which is usually a bilateral disorder, is characterized by the deposition of pigment granules on the corneal endothelium in a vertical pattern (Krukenberg spindle) and anterior chamber structures such as TM, iris, lens surface, and zonules [4, 5, 35]. These granules, which are welded iris pigment epithelial cells, cause an IOP elevation by increasing TM outflow resistance. Iris pigment release occurs as a result of mechanical contact between the posterior surface of the iris and the lens zonules [4, 5, 51, 52]. The cause of the classical finding, the midperipheral iris transillumination defect, is this contact. The trabecular endothelial cells phagocytose these granules, and the macrophages clear away these necrotic cells from the TM. Loss of trabecular endothelial cells secondary to denudation, collapse, and sclerosis of TM will cause a further increase in the outflow resistance and lead to the development of pigmentary glaucoma (PG) [5, 53–55].

The exact reason for pigment dispersion is not fully understood. However, there are some studies showing that genetic predisposition plays a role in this ocular disorder. Anderson et al. [56] identified a significant linkage between the PDS phenotype and chromosome 7 (7q35–36). Chang et al. [57] found a mutation on chromosome 6 in mice which develop pigment dispersion and iris stromal atrophy.

Classification [4, 58]

It can be classified into three groups:

(a) Pigment dispersion syndrome (PDS): It is characterized by dispersion of the iris pigment.
(b) Pigmentary ocular hypertension (POH): PDS with increased IOP and without glaucomatous optic neuropathy.
(c) Pigmentary glaucoma (PG): Glaucomatous optic neuropathy associated with PDS. It is one of the secondary causes of open-angle glaucoma.

Risk Factors

There is no comprehensive, multicenter, big sample size study identifying the risk factors and the rate of progression from PDS to PG, exactly. In the literature, the risk of progression to PG from PDS has been reported with various proportions.

The progression rate was found as 37.5% at the mean 4.2-year follow-up in 24 patients by Gomez Goyeneche et al. [59], 18% at the mean 2.3-year follow-up in 32 patients by Richter et al. [60], 35% at the mean 17.2-year follow-up in 65 patients by Migliazzo et al. [61], 10% at the mean 5-year follow-up, and 15% at the mean 15-year follow-up in 113 patients by Siddiqui et al. [62] Contrary to the progression rate, there is a consensus in the literature about the risk factor for progression to PG. Most of the studies declared that having a IOP > 21 mmHg at the time of diagnosis was the most important factor associated with progression. Family history of glaucoma, male gender, myopic refractive errors, presence of a Krukenberg spindle, and dense trabecular hyperpigmentation are the other contemplated risk factors.

Clinical Presentation and Signs

PG is most commonly seen in myopic Caucasian males between the ages of 30 and 50 years. Women tend to develop PG 10 years later compared to men [4, 5, 35]. Patients are mostly asymptomatic. Presentation of PG is usually as a moderate to severe stage of glaucoma in one eye and relatively mild damage in the fellow eye. Wide fluctuations in IOP levels may be seen. Higher levels of pressure may be observed in untreated patients or in case of sudden release of pigment granules, and patients can present to the emergency service with the complaints of acute pain in the eye, blurred vision, and headache. Pupillary dilatation [63], physical exercise [64–66], blinking [67], and accommodation [68] can trigger the pigment granule release. It should be considered that the findings and symptoms of patients with PDS/PG can decrease with aging. Campell [69] showed that the increase in axial length of the lens with age moved the iris forward and lifted the peripheral iris away from contact point of the lens-zonule bundle. Reduction in accommodation, pupil diameter, and iris pigment dispersion with aging may also contribute to this condition [35].

PG may develop after complicated cataract surgery associated with intraocular lens (IOL) implantation in the ciliary sulcus [70]. It should be considered that these patients may present with acute IOP elevation during both early and late postoperative periods.

The following findings are noted in the ophthalmic examination of many patients with PDS/PG:

- Vertical spindle-shaped pigment deposits (Krukenberg spindle)
- Very deep anterior chamber
- Melanin pigments floating in the aqueous
- Classic spokelike iris transillumination defect
- Posterior bowing of the iris with reverse pupillary block configuration
- Pigment deposits on the anterior and posterior lens capsule and on the lens zonules (Scheie's line)
- Wide open angle
- Characteristic heavy homogeneous hyperpigmentation on the TM and Schwalbe line.

Management

The management of PDS/POH/PG should be made according to the condition and activity of the patient.

- **Medical Treatment**

It is not different from that of POAG. Pilocarpine, which has specific anti-PDS effects, is an ideal treatment agent for PG. [58] It decreases the IOP level by increasing trabecular outflow, provides miosis, prevents the exercise-induced pigment dispersion, and reverses the mechanism of PDS formation by turning back the posterior iris bowing [5, 52, 64, 65, 69]. However, there are numerous adverse effects of pilocarpine which limit its long-term use, such as accommodative spasm, miosis, peripheral retinal detachment, cataract formation, visual symptoms, headache, and systemic parasympathomimetic effects [4, 5]. The use of other antiglaucoma agents is similar to that of POAG, because they have no additional effects for PDS. Although prostaglandin analogues increase iris pigmentation, they do not lead to an increase in pigment dispersion because they mainly affect the melanocytes in the iris stroma, not the pigment epithelium [71].

- **Laser Treatment**

There is no consensus on the effectiveness of laser iridotomy in patients with PDS/PG. Gandolfi and Vecchi [72] performed unilateral laser iridotomy to 21 patients with bilateral PDS. They observed IOP elevation more than 5 mmHg in 11 untreated eyes and 1 treated eye during the 2-year follow-up period. Pavlin et al. [73] investigated the laser iridotomy effect in patients with PG/PDS by ultrasound biomicroscopy. They indicated that concave iris attained a planar configuration after laser iridotomy. However, according to outcomes of a current meta-analysis, there is no sufficient evidence for the effectiveness of laser iridotomy in PDS/PG [74]. However, in PDS/PG patients with physical exercise-induced acute elevation of IOP, laser iridotomy may be preferred as the first treatment option [4, 73].

It is well-known that laser trabeculoplasty is an effective and repeatable treatment modality in PG [4, 5, 75–77]. Success rate is higher in PG because the TM of patients are hyperpigmented. Younger patients also have a higher success rate than older ones [75]. However, effectiveness wears off in time [4, 5]. It should be considered that at least one-third of patients will need a filtering surgery within 5 years of laser trabeculoplasty [75].

- **Surgical Treatment**

Trabeculectomy is performed as an effective and safe procedure for PG patients unresponsive to medical and laser treatments [5, 78]. Since the patients with PG are relatively young and myopic, extreme caution for hypotony maculopathy is required [79]. If the reason of PG is an IOL in the ciliary sulcus, its removal may be required in order to control the IOP levels.

7.3.4 Hyphema

7.3.4.1 Definition

Hyphema is an ocular condition which is characterized by the presence of hemorrhage in the anterior chamber. Hemorrhage often develops after ocular trauma as a result of vessel rupture in the peripheral iris and anterior ciliary body or angle distortion [80, 81]. It can be also seen after intraocular surgeries, or it may occur spontaneously associated with some ocular disorders (juvenile xanthogranuloma, rubeosis iridis, microhaemangiomas of iris, uveitis, malignancy), some systemic conditions, and the use of anticoagulant drugs (warfarin sodium) [82–87].

Traumatic hyphema is often a transient and self-limiting ocular pathology that may be managed conservatively [5, 88]. However, a number of patients, particularly in ones who rebleed, may experience complications such as elevated IOP and glaucoma and blood staining of the cornea. Rebleeding usually occurs 3–7 days after the initial ocular trauma with a 4–10% incidence [5, 35, 89–93]. Although the risk of rebleeding was shown to be related with certain factors such as hyphema size [90, 93], race [94], bleeding disorders [95], decreased BCVA [96], and elevated IOP [96], Kearns [89] did not observe any risk factor for rebleeding.

IOP elevation is the most common complication in patients with traumatic hyphema. Rahmani et al. [96] reported that IOP was higher than 21 mmHg in 14% of the patients with traumatic hyphema at initial admission. Furthermore, this ratio was found to be increased to 24% in patients who developed rebleeding. Türkcü et al. [91] declared that 35% of the children with serious hyphema following blunt ocular trauma had an IOP higher than 21 mmHg. IOP elevation occurs as a result of obstruction in the TM with red blood cells, platelets, and inflammatory cells in the acute period following ocular trauma [3, 35, 94, 97, 98]. There may be an increased incidence of IOP elevation in patients with sickle cell trait because the sickled erythrocytes pass through the TM with more difficulty [35, 88]. They are also at risk for optic nerve ischemia due to the already compromised microvascular perfusion [35].

Corneal blood staining is a relatively rare complication of hyphema. It is associated with high IOP levels, rebleeding, big hyphema size, and long clot duration, and it may lead to permanent endothelial decompensation [97–100]. Brodrick [99] determined the incidences of corneal blood staining as 2.1%, 22.2%, and 33.3% in 289 patients with traumatic hyphema, in ones

who developed rebleeding, and in ones who developed total rebleeding, respectively.

7.3.4.2 Risk Factors

It is well-known that the risk of complications is most strongly associated with the extent of hyphema. It was graded firstly by Agapitos et al. [92] as follows:

- Microscopic: There is no clot in the anterior chamber on slit-lamp examination.
- Grade 1: There is a gross clot occupying less than one-third of the anterior chamber.
- Grade 2: There is a gross clot occupying greater than one-third and less than one-half of the anterior chamber.
- Grade 3: There is a gross clot occupying more than one-half of the anterior chamber.
- Grade 4: Total clotted blood in the anterior chamber; it is named often as “eight ball” or “black” hyphema.

A grade of 2 or lower was shown to be associated with a 4% incidence of IOP elevation, a 22% incidence of complications, and a final BCVA of >6/18 in 78% of eyes, whereas a grade higher than 2 was associated with an 85% incidence of IOP elevation, a 78% incidence of complications, and a final BCVA of >6/18 in only 28% of eyes [5]. Patients with grade 4 hyphema carry a 100% risk of IOP elevation [98].

7.3.4.3 Clinical Presentation and Signs

The incidence of traumatic hyphema is reported to be 17 per 100,000 per year in children [92]. Kennedy and Brubaker [93] estimated the mean annual incidence of traumatic hyphema as 20.2 per 100,000 in males and 4.1 per 100,000 in females.

The patients with hyphema can present with blurred vision with or without eye pain and concomitant ocular trauma-related complaints. Although gross hyphema can be detected by penlight examination easily (Fig. 7.4), a careful slit-lamp examination is required in order to detect microhyphema (Fig. 7.5).

It is well-known that the final BCVA of patients’ traumatic hyphema is related to accompanying anterior and posterior segment complications such as traumatic cataract, iridodialysis, angle recession (Fig. 7.6), glaucoma, vitreous hemorrhage, and peripheral retinal tear. Therefore, the ophthalmic examination should be performed in detail (including gonioscopy if possible) and in a suitable time. Ophthalmologists should also be gentle during the indirect peripheral fundus examination (provided that there is no contraindication).

7.3.4.4 Management

The aim of the treatment is to accelerate the absorption of hyphema in the anterior chamber and to avoid the complications. First of all, the complete medical history of the patient including medications, ocular and systemic disorders, and details of trauma must be obtained. The other problems induced by trauma must be iden-

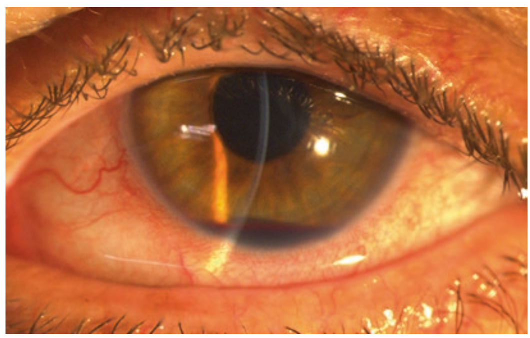

Fig. 7.4 A grade 1 hyphema, which may be detected with penlight examination, is observed in an otherwise healthy appearing eye

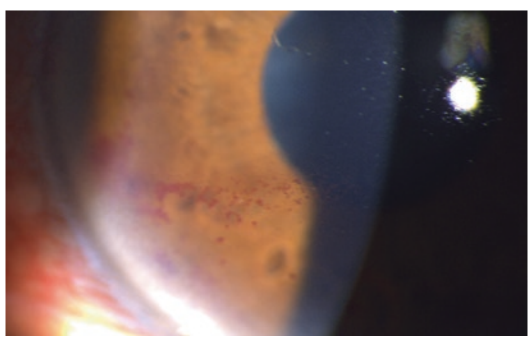

Fig. 7.5 In contrary to a gross hyphema, the microhyphema in this case may be easily unnoticed with penlight examination and requires a careful slit-lamp exam for diagnosis

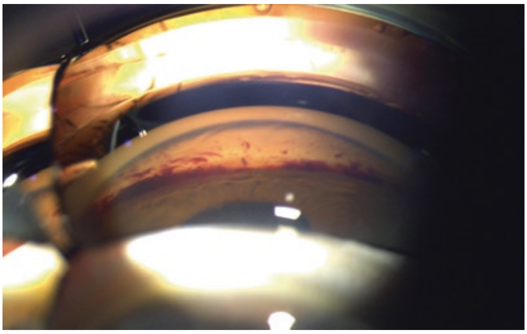

Fig. 7.6 Gonioscopic examination of this eye in the first few days after trauma revealed angle recession and hyphema in the angle

tified by a detailed slit-lamp examination. The ophthalmologists should be more careful for patients with bleeding diathesis and for pediatric patients.

- **Medical Treatment**

The patients with uncomplicated hyphema are managed conservatively with bed rest, head elevation, and eye patching. These measures decrease the rebleeding risk, promote visual rehabilitation, prevent clot formation in the pupilla, increase patient comfort, and heal corneal abrasions. The patients who have large hyphema may need to be hospitalized.

The cessation of the anticoagulant and antiplatelet medications is a controversial issue.

Consultation with the patient's family physician must be absolutely made before the decision to cease these medications because the most common indication for these drugs is cardiovascular disorders. Crawford et al. [101] showed that the rebleeding rate was statistically significantly higher in patients treated with aspirin (39% vs 4%). Antifibrinolytic agents such as tranexamic acid and aminocaproic acid can be used in order to decrease the rebleeding rate after hyphema. Most of the studies have shown that systemically and topically used antifibrinolytics reduce the incidence of rebleeding in patients with hyphema [88, 102–104]. Rahmani and Jahadi [104] investigated the effect of tranexamic acid and prednisolone on rebleeding in patients with severe hyphema during the hospital course in a placebo-controlled clinical trial. They observed statistically significantly lower incidence of rebleeding in the tranexamic acid group compared to the placebo group. However there was no statistically significant difference between tranexamic acid and prednisolone groups. Similarly, Albiani et al. [105] found that children with hyphema treated with combined tranexamic acid and topical steroids did not have a statistically significantly lower rebleeding incidence than those treated with topical steroids alone. It should be considered that the use of antifibrinolytic agents may cause a delay in clot resorption [88].

Topical mydriatics or cycloplegics decrease the risk of posterior synechiae formation, relieve the discomfort in patients with concurrent iritis, and permit fundus examination. There is no effect on rebleeding or the final BCVA [88, 106].

To control the high IOP, antiglaucoma medication should be used. A hyperosmotic agent, a β-blocker, an α-agonist, and/or a topical or systemic carbonic anhydrase inhibitor (not in sickle cell trait) may be administered according to IOP levels. Prostaglandins should not be used because they increase inflammation, and the miotics should not be used because they break down the blood-aqueous barrier and cause pupillary block [5].

Topical steroids decrease posterior synechiae formation by reducing inflammation in patients with hyphema. They can also strengthen the blood-ocular barrier and decrease the rebleeding rate [107]. Some authors recommend an oral steroid treatment, which is named as the Yasuna protocol, and abovementioned measures for all patients with hyphema [107, 108]. Farber et al. [109] compared the efficacies of oral aminocaproic acid and oral prednisone in reducing the rate of rebleeding in patients with hyphema in a randomized clinical trial and determined that the two groups had an equal rebleeding rate. However, no consensus regarding management of hyphema exists. Hence, the medical treatment of hyphema has been named as a "continuing controversy" in the literature, because many clinical trials have been criticized for their poor science and poor scientific methods.

- **Surgical Treatment**

Surgical treatment may be preferred in patients with hyphema at high risk for sight-threatening complications [98]. However, some authors found that the surgically treated patients with hyphema had worse final BCVA and higher complication rates [94, 110]. Read [110] recommended that medical treatment should be preferred to surgical treatment during the initial 4 days, even in patients with major hyphema. A high IOP level and presence of corneal blood staining are prerequisites for surgical treatment. Surgical treatment is also suggested for the following conditions: [110]

– Total hyphemas with IOP ≥ 50 mmHg for 5 days
– Total hyphema that fails to resolve to below than the half of the anterior chamber at 6 days with IOP ≥ 25 mmHg
– Hyphema that remains unresolved for 9 days

The most commonly used surgical approach is anterior chamber washout with a Simcoe or irrigating-aspirating cannulas or a vitrectomy probe. Trabeculectomy with anterior chamber washout and peripheral iridectomy may be required if other treatment modalities fail [111]. Some surgeons perform trabeculectomy as the initial surgical treatment in order to reduce the high IOP level immediately [35].

In conclusion, the majority of patients with hyphema heal smoothly and uneventfully. However, severe complications related to the hyphema and/or ocular trauma itself may be encountered. It should also be kept in mind that prolonged hypema and corneal blood staining may lead to deprivation amblyopia in children.

7.4 Scleritis

Definition

Scleritis, which is a severe inflammatory condition of the sclera, was classified first by Watson and Hayreh based on the anatomical location into the following categories: [112]

- Anterior scleritis
  (a) Diffuse scleritis
  (b) Nodular scleritis
  (c) Necrotizing scleritis
    (i) With inflammation
    (ii) Without inflammation (scleromalacia perforans)
- Posterior scleritis

Although scleritis has a wide spectrum of etiologic factors, it is crucial to determine whether the etiologic factor is infectious or not. Approximately half of the cases with anterior scleritis are related to autoimmune diseases such as rheumatoid arthritis (RA), systemic lupus erythematosus, Wegener's granulomatosis, polyarteritis nodosa (PAN), and seronegative spondyloarthropathies, whereas the cause of scleritis is infectious in 5–10% of patients [113–117]. Especially, RA is the most commonly seen connective tissue disease in association with scleritis [116, 118]. However, the exact reason cannot be determined in many of the patients (idiopathic). Rarely, scleritis can be seen months to years after an ocular injury or surgery by activating an inflammatory response [119].

Clinical Presentation and Signs

Scleritis, which actually is a rare ocular disorder, is mostly seen in women aged 40 to 60 years [116, 118, 120–124]. Honik et al. [121] found the overall incidence of scleritis as 3.4 per 100,000 person-years in a large population-based study. Clinical presentation varies according to the type of scleritis.

- **Diffuse anterior scleritis:** It is the most commonly seen type, accounting for 45%–61% of all scleritis cases [118, 122]. The patients present with redness and acute pain in the eye. The ocular pain is severe and typically increases at night and wakes the patient from sleep, and it may spread to the face, cheek, and jaw.[5123] The eye is also sensitive to palpation, and this aids to differentiate it from uveitis. The patients with accompanying uveitis may also complain of photophobia, epiphora, and blurred vision. Diffuse anterior scleritis is more common in

women in the fifth decade. The visual acuity of patients with anterior scleritis is usually normal [123]. Intense redness due to congestion of the blood vessels and edema of the sclera is easily determined by macroscopic and slit-lamp examination. The phenylephrine test can be used to differentiate from episcleritis. After installation of topical phenylephrine, conjunctival redness does not disappear in patients with scleritis. The cornea may be involved in patients with severe scleritis, which presents as peripheral corneal infiltrates characterized by small white lesions, corneal thinning, and ulceration [124].

- **Nodular anterior scleritis:** It presents as a single or multiple immobile nodules of scleral edema and vascular congestion. Scleral nodules which are deep red-purple in color and separated from the overlying episcleral tissue develop mostly in the interpalpebral area 3–4 mm away from the limbus [5, 120]. The slit beam of the slit lamp is displaced due to the scleral nodule in ophthalmic examination. Multiple nodules may rarely become confluent by expansion, and the sclera may become apparent due to increased translucency as the nodule subsides. Most of the nodules heal by developing a small atrophic scar in their center. However if treatment is delayed, approximately 10% of patients may develop necrotizing scleritis [5].
- **Anterior necrotizing scleritis with inflammation:** Necrotizing scleritis, which is the most destructive form of scleritis, is characterized by intense vasculitis [119, 125] that leads to scleral necrosis by occlusion of the deep episcleral vascular plexus. It presents at older ages compared to other types of scleritis. Patients often present with severe ocular pain. A localized patch of scleral inflammation and necrosis can be seen initially. If untreated it may spread to posterior ocular structures and can progress to exposure of the choroid. In this case, the sclera thins and the underlying uveal tissues become visible as blue-gray in color. Anterior necrotizing scleritis with inflammation can lead to many ocular complications including acute keratitis, uveitis, glaucoma, hypotony, and perforation. Necrotizing scleritis may be a sign of a potential threat, not only to eyesight but also to life [125]. There are three subtypes of anterior necrotizing scleritis with inflammation: [5] *vaso-occlusive* subtype is often associated with RA, *granulomatous* subtype is often associated with Wegener's granulomatosis and PAN, and *surgically induced* subtype often starts within 3 weeks of the ocular surgery.
- **Anterior necrotizing scleritis without inflammation (scleromalacia perforans):** It occurs as a result of an obliterative arteritis of the deep episcleral vascular plexus [119, 122]. It is often seen in elderly women with long-standing RA. Since inflammation does not accompany scleromalacia perforans, the patients are typically asymptomatic, or they sometimes present with nonspecific irritation or dry eye complaints [5]. Vascular congestion is absent and the visual acuity is usually normal. Sometimes, astigmatism can be seen due to advanced scleral thinning. A blue-gray sclera due to slow scleral thinning and exposure of underlying uveal tissues is observed (Fig. 7.7). Spontaneous globe perforation or after minimal trauma can rarely develop in chronic cases.
- **Posterior scleritis:** The inflammation is settled posterior to the insertion of the rectus muscles. It develops less frequently and it is mostly seen in younger age than those with isolated anterior scleritis [118, 126]. Gonzalez-Gonzalez et al. [126] compared the clinical characteristics of 31 patients with posterior scleritis and 469 patients with anterior scleritis. They found the mean ages of patients as 43.6 vs. 54.4 years, respectively, and the rates of decreased visual acuity as 29.0% vs. 14.9%, respectively [126]. Patients may present with ocular pain, proptosis, diplopia, blurred vision, and limitation of ocular movements [112, 119, 123]. Eyelid (especially lower eyelid) retraction secondary to infiltration of muscles can occur. Exudative retinal detachment,

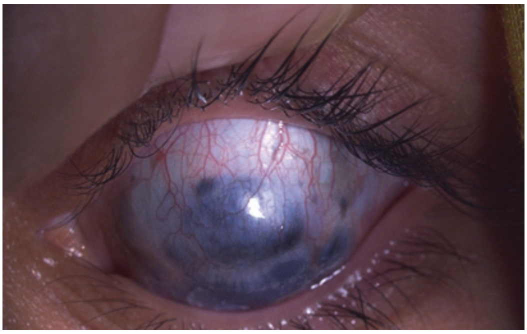

Fig. 7.7 Anterior segment examination of this eye in down gaze discloses markedly thinned sclera superiorly. Hence, underlying uveal tissues, both the choroid and the ciliary processes, are visible under the extremely thinned sclera

swelling of the optic disc, choroidal folds, and uveitis can be detected in ophthalmic examination. B-scan ultrasonography (T sign), computerized tomography (CT), or magnetic resonance imaging (MRI) may be helpful in confirming the diagnosis of posterior scleritis by determining the thickened sclera. It should be kept in mind that posterior scleritis may occur in isolation, or it may be accompanied by anterior scleritis.

- **Infectious scleritis:** Many causative agents for infectious scleritis such as bacteria, fungi, parasites, and viruses are present. Jain et al. [117] found the most common etiological agent as fungus in a developing country, whereas Hodson et al. [127] found it as *Pseudomonas aeruginosa*. Ocular surgery or trauma can be a promoting factor for infectious scleritis. It can develop days to years after ocular surgeries [115, 119, 127]. Presentation of patients with infectious scleritis can be similar to the other types of scleritis. Consequently, these patients may be given corticosteroids, which often worsen the clinical course of infectious scleritis. Taking cultures or biopsies is important for diagnosis in case of clinical suspicion. Destructive effects of the causative organism also play a negative role in the visual outcome of the patients. Unfortunately a useful vision (BCVA $\geq$ 20/200) cannot be preserved in the majority of the cases [115, 117, 127]. Hodson et al. [127] determined that poor visual acuity at presentation and the presence of keratitis or endophthalmitis were associated with poor vision outcomes in 56 patients with infectious scleritis.

Management

- **Treatment of immune-mediated scleritis**

Firstly, all patients require a systemic evaluation because scleritis may be the first manifestation of an autoimmune disorder. In this way, we can not only save the patients' vision but also their life.

Topical corticosteroids and systemic NSAIDs can relieve the symptoms in mild cases of non-necrotizing disease by reducing the inflammation and edema [5, 114, 119]. However, a systemic corticosteroid treatment is required in necrotizing and posterior scleritis. Periocular steroid injections can be applied safely in selected patients with non-necrotizing anterior scleritis [114, 128, 129]. When the systemic steroid response is inadequate or it has to be discontinued, immunosuppressive agents (methotrexate, cyclophosphamide, azathioprine, mycophenolate mofetil) and immunomodulators (ciclosporin, tacrolimus) are recommended [5, 114, 119]. Although there is no consensus, immunosuppressive drugs are often preferred in scleritis with underlying autoimmune diseases [119]. Recent studies indicate that the biological agents (infliximab, adalimumab, etanercept) can be an effective treatment modality for scleritis refractory to corticosteroids and immunosuppressive treatments [130–133].

- **Treatment of infectious scleritis**

Early diagnosis and appropriate medical treatment is crucial especially in patients with infectious scleritis. Ophthalmologists should be suspicious for an infectious cause, especially in patients with scleritis who are refractory to corticosteroids and immunosuppressive therapies. The most common initial signs of infectious scleritis are scleral abscess and necrosis [115]. If required surgical debridement should not be avoided. Tittler et al. [134] reported the positive outcome of antibiotic therapy and early scleral debridement in 13

patients with infectious scleritis. In contrast to the poor outcomes of infectious scleritis cases in the literature, no patient required enucleation in their series. Corticosteroid treatment in infectious scleritis remains a controversial issue. Although corticosteroids are well-known to reduce inflammation, many ophthalmologists avoid using them in infectious scleritis. We believe that they can be used under close monitoring together with the appropriate antimicrobial treatment.

7.5 Uveitis

Definition

Uveitis is a sight-threatening ocular inflammatory disease classified as anterior, intermediate, posterior, and panuveitis according to localization of this inflammation by Standardization of Uveitis Nomenclature Group in 2005 [135]. It can also be classified as acute, chronic, and recurrent according to the clinical course, as granulomatous or non-granulomatous according to clinical appearance, and also as infectious and noninfectious according to etiology.[5137–140] Infectious causes are common in the developing countries, whereas they are rarely seen in the developed world. In the overall, anterior uveitis is the most common form of uveitis [136–142]. Prevalence and cause of uveitis vary widely from country to country. Chang et al. [143] found the annual incidence rate of acute anterior uveitis to be approximately 36 cases/100,000 in a prospective observational study in Central Australia. In another study, the mean annual incidence rate of idiopathic acute anterior uveitis was found as 17 cases/100,000 population in Finland [144].

Only acute anterior uveitis will be addressed in this section, because it is the most common uveitis associated with acute pain in the eye. The pain of acute anterior uveitis results from the iris inflammation (iritis) and/or IOP elevation [136]. The pain may also radiate to a larger facial area supplied by the trigeminal nerve.

Clinical Presentation and Signs of Acute Anterior Uveitis

The patients with anterior uveitis have a range of presentation from a painless white eye to an extremely painful red eye [5]. The pain is often with sudden onset and unilateral. Photophobia and lacrimation may accompany the pain. Visual acuity of patients with isolated acute anterior uveitis is usually normal initially except in eyes with severe inflammation and/or hypopyon. Ciliary injection is easily seen by external examination with daylight. The following findings may be noted on ophthalmic examination of patients with acute anterior uveitis:

- Endothelial dusting or fine keratic precipitates (Fig. 7.8)
- Miosis because of sphincter spasm
- Cellular reaction in the anterior chamber (the cells may also be present in the anterior vitreous)
- Posterior synechiae (Fig. 7.9)
- Low IOP because of reduced secretion of aqueous humor by the ciliary epithelium or high IOP

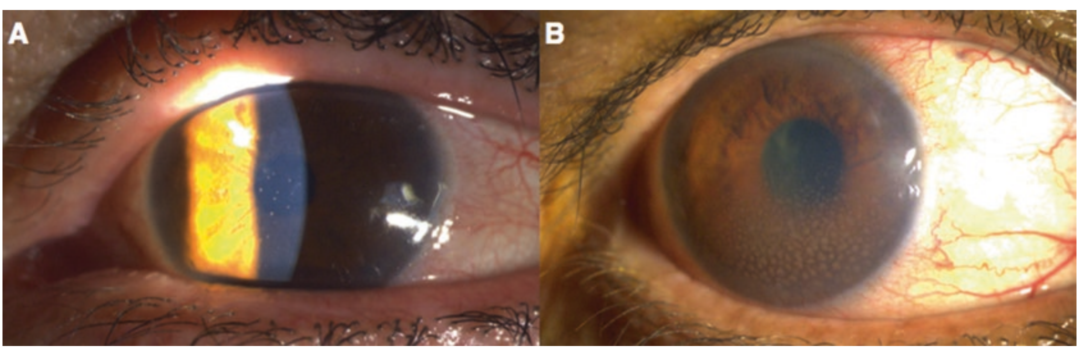

Fig. 7.8 (**a**) Fine keratic precipitates are demonstrated in this slit-lamp photo. (**b**) The large greasy keratic precipitates of granulomatous uveitis are named as “mutton fat”

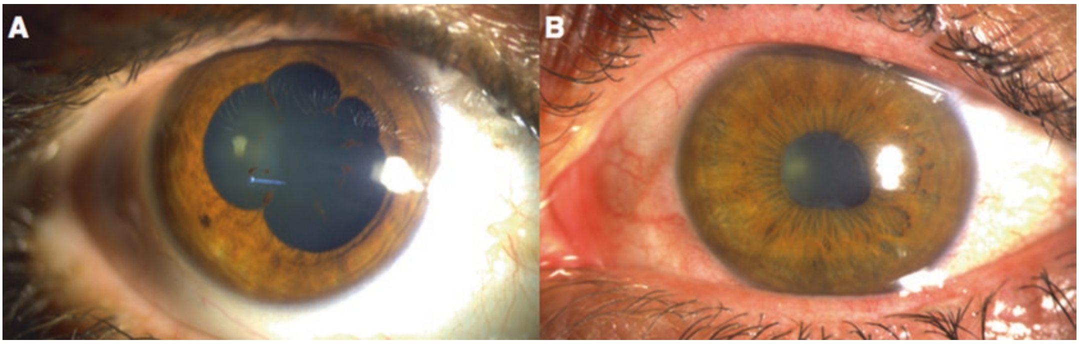

Fig. 7.9 (**a**) Pupillary synechiae in this eye have led to an irregular pupillary appearance upon dilatation with mydriatic drops. Also note the iris pigment remnants on the lens at 3–5 o'clock positions, which indicate previous synechiae which probably have resolved with mydriatics. (**b**) This slit-lamp photo demonstrates almost total posterior synechia except for the 4–5 o'clock positions

because of trabeculitis particularly in herpetic uveitis and Posner-Schlossman syndrome

Management

Treatment of immune-mediated anterior uveitis includes topical corticosteroids and a mydriatic or cycloplegic agent [5]. Clinicians should absolutely investigate the patient's systemic involvement especially in terms of underlying disorders.

Corticosteroid therapy is the mainstay of uveitis management. It reduces the active inflammation and prevents or treats the complications of uveitis including cystoid macular edema. Initially topical steroid instillation should be started hourly, and then it should be tapered gradually according to severity of inflammation. It should be kept in mind that the long-term steroid treatment may result in IOP elevation and cataract, and also the clinical course of infectious uveitis may be affected adversely.

Topical mydriatic or cycloplegic agents not only prevent or break down the posterior synechiae formation but also relieve the pain and photophobia secondary to ciliary spasm.

7.6 Endophthalmitis

Definition

Endophthalmitis is characterized by devastating inflammation of intraocular tissues and is the most feared complication of intraocular surgeries although it is seen rare [145–148]. The majority of the studies in literature are related to endophthalmitis seen after cataract surgery. Jabbarvand et al. [145] and Lundström et al. [146] found the incidence of endophthalmitis as 0.023% and 0.035% in 480,104 and 692,786 patients who underwent cataract operations, respectively. Endophthalmitis is classified as exogenous and endogenous according to the entry location of the agent. Exogenous endophthalmitis is caused by inoculation of a microorganism from the external environment, whereas endogenous endophthalmitis develops by hematogenous spread of a microorganism from any region of the body.

Endophthalmitis can also be classified as acute-onset and chronic (or delayed-onset) postoperative endophthalmitis according to time of onset. Acute-onset endophthalmitis is generally defined as developing within 4–6 weeks of an intraocular surgery, whereas delayed-onset endophthalmitis has an onset ranging from 4 to 6 weeks to years [5, 136, 149, 150]. Only acute-onset postoperative endophthalmitis will be addressed in this section because it is the subtype most often characterized by acute pain. Delayed-onset endophthalmitis usually occurs because of a low virulence organism such as *P. acnes* trapped in the capsular bag, and it mostly presents with painless mild visual loss.

Risk Factors

Currently, the incidence of acute endophthalmitis following cataract surgery has decreased to 0.3% through advances in surgical techniques and equipments [5]. There are some well-known risk factors for endophthalmitis following cataract surgery such as posterior capsule rupture, prolonged operation time, clear corneal incision, temporal incision, adnexal disease, and diabetes mellitus. Jabbarvand et al. [145] found a statistically significant association of endophthalmitis with diabetes mellitus, older age, vitreous loss, extracapsular cataract surgery, and interestingly surgery on the left eye in a series of 480,104 cataract operations. They did not find an association between the endophthalmitis risk and the surgeon experience. Lundström et al. [146] determined the following three groups at risk for endophthalmitis in a series of 692,786 cataract operations: lack of treatment with intracameral antibiotics, vitreous loss, and age older than 85 years.

The source of endophthalmitis is usually the flora of the eyelids and conjunctiva. Much rarely, it may be external factors such as contaminated solutions and equipments, the surgeon, and the staff.

Although the exact pathogen may not be identified in some cases, mostly (90%) Gram (+) bacteria including coagulase-negative *Staphylococci*, *S. aureus*, and *Streptococcus species* and rarely (10%) Gram (−) bacteria including *Pseudomonas* and *Proteus* species can be isolated [5].

Fig. 7.10 In this eye presenting with postoperative endophthalmitis 1 day after cataract surgery, marked ciliary injection, central corneal edema, and a dense hypopyon inferiorly in the anterior chamber are observed. Also note the clear corneal incision at the 11 o'clock, which probably is the entry site for the infectious agent in this case

Clinical Presentation and Signs

The patients with acute-onset postoperative endophthalmitis often present with vision loss, severe pain, and redness in the eye. According to the Endophthalmitis Vitrectomy Study (EVS) which was a multicenter, randomized clinical trial evaluating 420 patients who had clinical evidence of endophthalmitis within 6 weeks after cataract surgery or secondary IOL implantation, decreased visual acuity was observed in 94% of patients, conjunctival injection in 82% of patients, eye pain in 74% of patients, and eyelid edema in 35% of patients [151]. On ophthalmic examination of patients with acute endophthalmitis, decreased BCVA, eyelid swelling, corneal edema, conjunctival injection and chemosis, discharge, hypopyon, vitritis, and loss of the red reflex may be determined (Fig. 7.10) [5]. The findings vary according to causative agent and severity of endophthalmitis.

Management

The management should be performed according to the course and severity of endophthalmitis upon the presentation of patients. Endophthalmitis patients should be followed closely and energetically. The mild cases are generally administered with intravitreal, subconjunctival, topical, and oral antibiotic treatments, whereas the severe cases occasionally require pars plana vitrectomy. Although the EVS [151] found that the vitrectomy procedure provided significantly better visual outcomes only in the eyes with a visual acuity of perception of light at presentation, it should be kept in mind that the vitrectomy techniques and instruments have developed groundbreakingly since the time of the study (1995). Consequently, many retina surgeons prefer to perform vitrectomy in a much earlier period in endophthalmitis cases.

Intravitreal antibiotic treatment, which usually includes a two-antibiotic combination, plays a crucial role in the management of the endophthalmitis. Vancomycin (2 mg/0.1 mL) for Gram (+) microorganisms and ceftazidime (2 mg/0.1 mL) or amikacin (4 mg/0.1 mL) for

Gram (−) microorganisms constitute the most commonly used combination. A 25-G needle is used for intravitreal injection. Topical and subconjunctival antibiotic (vancomycin and ceftazidime) applications have a limited additional benefit. The topical and oral use of the third- or fourth-generation fluoroquinolone can be also preferred because they achieve effective levels in the aqueous and vitreous. If a causative agent can be detected in aqueous or vitreous samples, the treatment can be changed.

Although corticosteroids can decrease the destructive intraocular inflammatory response to the infectious agent, their intravitreal or oral use is a controversial issue. It should never be used if a fungal pathogen is suspected.

Subsequent management should be planned according to the response to the treatment. The treatment should not be changed if there is an improvement in the clinical findings. If the clinical findings deteriorate, intravitreal antibiotic injection should be repeated after 2 days, or vitrectomy may be considered. Reinjecting amikacin intravitreally is not recommended due to its retinal toxicity [5].

Poor visual outcome is inevitable in many endophthalmitis cases. The visual loss results from damage caused by the toxins and proteases of microorganisms and by the inflammatory response of the host to the infection. It may even result in loss of the eye despite an appropriate diagnosis and treatment [152].

It is well-known that prevention of endophthalmitis is always more effective and logical than treating it. There is a consensus on instillation of 5% povidone iodine onto the ocular surface for 5 min at the beginning of surgery and the administration of intracameral antibiotics at the end of the surgery. Nowadays, these are considered as the most effective measures in order to prevent endophthalmitis among cataract surgeons. Jabbarvand et al. [145] declared that they did not observe any case of endophthalmitis among the 25,920 patients who received intracameral cefuroxime (1 mg in 0.1 mL).

See Chap. 8 for more detailed information about endophthalmitis.

7.7 Corneal Abnormality

Definition

The cornea, which is a crucial component of the ocular refractive power, protects the eye as a barrier against infection and trauma. Most of the corneal disorders result in acute eye pain, because the cornea is one of the most sensitive tissues in the body in terms of nociception. Consequently, the most common ocular diseases presenting at emergency service with eye pain are cornea-related diseases such as corneal abrasion and corneal foreign body [153–156].

Risk Factors

Risk factors for corneal diseases are a history of trauma, contact lens overwear (Fig. 7.11), male gender with age between 20 and 34 years, construction or manufacturing occupation, and lack of eye protection [157–159].

Clinical Presentation and Signs

Presenting symptoms of corneal abnormality can be eye pain, watering, decreased visual acuity, photophobia, red eye, and foreign body sensation [157]. If the patient cannot tolerate the examination because of pain, a single drop of a topical anesthetic can be applied in order to facilitate ophthalmic examination by alleviating the ocular pain. On ophthalmic examination of patients, pathological findings such as corneal foreign

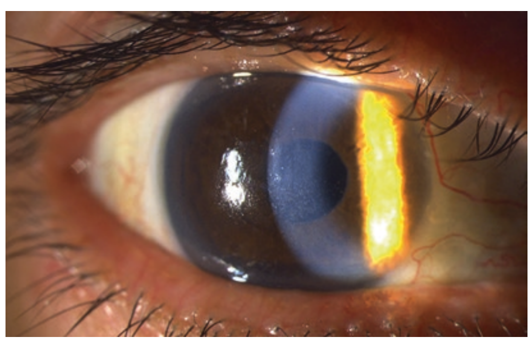

Fig. 7.11 In this eye, slit-lamp examination revealed punctate corneal epithelial defects, which was due to contact lens overwear for 10 days. With penlight examination, it was not possible to observe this subtle finding

bodies can be seen easily with a penlight. However, some corneal abrasion cases may not be noticed even with a slit lamp without fluorescein dye. Therefore, the use of fluorescein dye and careful examination are required in order to diagnose any occult corneal epithelial defect. It also helps the ophthalmologist in the follow-up examinations by documenting the depth and the size of corneal abrasions [156].

Management

The aim of treatment of patients with corneal abnormality is to provide corneal healing and symptomatic relief and to prevent bacterial superinfection. The mainstay of treatment is a combination of topical antibiotics and lubricating artificial tears [156]. Topical cycloplegics and/or oral NSAIDs can also be used for patients complaining of significant pain and discomfort. Patching for corneal abrasions is a controversial issue. Although most of the ophthalmologists often perform patching, recent studies have shown that patching had no advantage in terms of improving healing or reducing pain of patients with simple corneal abrasion [154].

It should be kept in mind that prevention of ocular injury is easier and more effective than treating the potential long-term complications.

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8 Open-Globe Injuries

Sengul Ozdek and Ece Ozdemir

Abstract

Open-globe injury is a significant cause of permanent vision loss worldwide. Besides inevitable psychological impacts on the patient and the family, it also places a severe socioeconomic burden on society, given the fact that young individuals are the mostly affected group.

Proper evaluation of the nature and extent of the injury and planning a management strategy are of utmost importance for prognosis in open-globe injuries. Wide spectrum of tissue injuries makes an open-globe injury a challenge to the surgeon. Thread of expulsive hemorrhage and endophthalmitis further complicates the situation.

Although initial damage cannot be undone, prompt and appropriate medical and surgical management may prevent further complications, resulting in more favorable outcomes.

This chapter provides a guide to emergency management of open-globe injuries, with emphasis on differences according to different types of injuries (e.g., lacerations, ruptures) and prevention and treatment of associated complications.

Keywords

Open globe injury · Primary wound repair · Post-traumatic endophthalmitis · Globe rupture · Intraocular foreign bodies

8.1 Introduction and Terminology

Ocular trauma results in a wide spectrum of tissue lesions, which are essential to be clearly defined for accurate transmission of clinical data and interpretation. Birmingham Eye Trauma Terminology (BETT) is a standardized classification system of terminology, designed to promote more uniform use of trauma-related terms [1] (Fig. 8.1).

BETT uses the entire globe as the tissue of reference. Open-globe injury by definition is a full-thickness defect of the eyewall (cornea and sclera) which is due to either laceration or rupture, depending on the inciting object's characteristics and mechanisms of injury.

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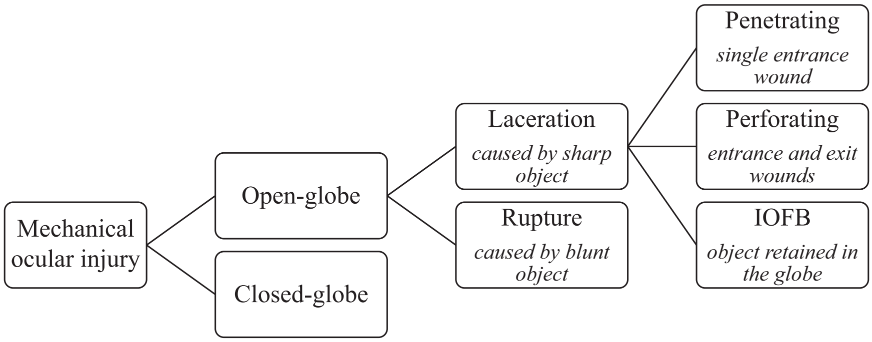

Fig. 8.1 Birmingham eye trauma terminology. *IOFB* Intraocular foreign body (Reproduced with the permission [102])

Table 8.1 Classification of the open-globe injuries

Type	Grade (VA)	Pupil	Zone
Rupture	≥20/40	Positive RAPD in the injured eye	I. Cornea and limbus
Penetrating	20/50 to 20/100	Negative RAPD in the injured eye	II. Limbus to 5 mm posterior into sclera
IOFB	19/100 to 5/200		III. Posterior to 5 mm from limbus
Perforating	4/200 to LP		
Mixed	NLP		

LP light perception, *NLP* no light perception
Reproduced with the permission [102]

8.1.1 Lacerations

Lacerations are full-thickness defects of the eyewall, caused by a sharp object with an outside-in mechanism.

Penetrating injury is a subtype of laceration which has a single point of entry into the globe, but no exit wound.

If the penetrating object is retained in the globe, it is classified as IOFB which is technically a penetrating injury but is grouped separately because of different clinical implications (see Sect. 8.3).

Perforating ocular injuries are “through-and-through” globe defects with entry and exit sites.

8.1.2 Ruptures

Ruptures occur by an inside-out mechanism; when a blunt object impacts the globe with a substantial momentum, it causes an elevation in the intraocular pressure to a point that the sclera tears with immediate extrusion of tissues.

8.1.3 Classification of the Open-Globe Injuries

The Ocular Trauma Classification Group developed a classification system that was based on BETT [2] (Table 8.1). This system includes four specific variables of ocular trauma that have been shown to be prognostic of final visual outcome:

1. Type of injury (based on the mechanism of the injury) [3–7]

   Blunt mechanisms have worse prognosis than the sharp injuries, with ruptures and mixed type injuries having the worst outcomes.
2. Grade of injury (based on the initial visual acuity) [3–5, 7–10]

   Initial visual acuity (VA) has been demonstrated to be the most reliable predictor of the final visual outcome in open-globe injuries [8–10]. A good VA on presentation is more likely to correlate with good final visual acuity.
3. Presence or absence of a relative afferent pupillary defect (RAPD) in the involved eye [3, 4, 7]

Table 8.2 Calculating the OTS[a]

Step 1. Determining the raw points	Variables					Raw points
	Initial vision					
	NLP					60
	LP/HM					70
	1/200–19/200					80
	20/200–20/50					90
	≥20/40					100
	Rupture					−23
	Endophthalmitis					−17
	Perforating injury					−14
	Retinal detachment					−11
	RAPD					−10
Step 2. Conversion of sum of raw points into the OTS for expected final visual outcome (%)						
Sum of raw points	OTS	NLP	LP/HM	1/200–19/200	20/200–20/50	≥20/40
0–44	1	74	15	7	3	1
45–65	2	27	26	18	15	15
66–80	3	2	11	15	31	41
81–91	4	1	2	3	22	73
92–100	5	0	1	1	5	94

[a]If a specific variable is not available, its value accepted as zero
Reproduced with the permission [95] and [102]

Presence of RAPD is related to unfavorable outcomes.

4. Zone of injury (based on the location of the wound) [3–5, 8]

Zone III injuries are related to worse outcomes when compared to zone I and II injuries.

8.1.4 Ocular Trauma Score

Kuhn and his colleagues developed the ocular trauma score (OTS), by analyzing more than 2500 eye injuries from the US and Hungarian Eye Injury Registries, in an attempt to provide an objective system for standardized assessment of ocular injuries and prognosis [11] (Table 8.2). Based on the characteristics of the injury (initial visual acuity, rupture, endophthalmitis, perforating injury, retinal detachment, RAPD) which are readily available at the time of the initial evaluation or surgery, the OTS gives the ophthalmologist a 77% chance to predict the eventual functional outcome within ± one visual category immediately after the injury [12]. Studies have shown that the OTS provides reliable prognostic information that allows the ophthalmologist appropriate counseling of the patient regarding prognosis [13, 14].

8.2 Emergency Management of the Open-Globe Injuries

8.2.1 Evaluation of Open-Globe Injuries

When a patient who had an ocular trauma is first seen, the presence of any life-threatening injuries should be ascertained prior to ophthalmic evaluation. Once it is confirmed that the patient is stabilized, the initial aim must be to determine the nature and extent of the ocular injury, so that the management can be optimally planned.

8.2.1.1 History

History should focus on the critical information that will guide the ophthalmologist to understand the extent of the injury without causing a delay in intervention.

The following details should be addressed:

- General circumstances where the injury has taken place
  - Rural setting and the possibility of soil contamination increase the risk of infection.
- Mechanism of the injury and characteristics of the causing agent which may alarm the surgeon about the probability of an occult rupture, retained IOFB(s), or retinal injury
  - Sharp objects usually cause lacerations with possible IOFBs whereas injury with blunt objects may result in occult ruptures.
  - In cases of injury with high-speed missiles or long sharp objects, retinal damage with possible perforating injury should be suspected.
  - Multiple IOFBs may be found if the injury is caused by an explosion.
- Time of the injury and the time the patient last ate or drank are important for planning the timing of the intervention
- Initial symptoms and change in symptoms
  - An increase in pain may suggest the development of endophthalmitis or severe intraocular hemorrhage.
- Prior ocular history
  - Previous ophthalmic surgery or trauma sites are predisposed to ruptures (see Sect. 8.2.7.2).
  - It is important for assessment of the preinjury vision and the potential of the eye.

8.2.1.2 Physical Examination

External Inspection

Using penlight and diffuse illumination, both periocular regions[1] and globes should be inspected for any major abnormalities and compared to the fellow eye.

- Inspect the periocular region for lacerations, hemorrhages, foreign bodies, and lid edema. Look for any bone asymmetry or step-off deformity that signals an orbital fracture.
- Compare the position of the eye with the fellow eye by looking at the patient's forehead from above to see if there is enophthalmos/exophthalmos.
- Gently palpate the periocular region for occult subcutaneous foreign bodies, crepitus, and infraorbital hypoesthesia.
- Inspect globe for wounds, any foreign bodies, prolapse of intraocular contents, and chemosis. Compare the anterior chamber depth with the fellow eye with a penlight.

Tip: It is critical not to exert pressure on the globe during examination. A speculum or Desmarres lid retractor may be used if there is severe lid edema. Ice packs and corticosteroid ointments can also help to reduce the edema. If a sufficient examination is not possible without the risk of extrusion of the ocular contents, the clinician should not hesitate to postpone the examination to the operating room under anesthesia.

Visual Acuity Assessment

- Visual acuity should be measured in each eye separately, using an occluder.
- The testing can be done at a distance using either the Snellen or ETDRS charts or illiterate charts (E, C charts) and at near with the Rosenbaum card. If vision is too poor to be measured with standard charts, gross assessment can be made (counting fingers at a given distance, hand motions, light perception with or without projection, and no light perception).
- When possible, all testing should be done with the patient's corrective lenses if available, if not pinhole can be used as a substitute.

Assessment of Pupillary Reflexes

Presence of a RAPD is a crucial prognostic factor that may indicate optic nerve damage or severe retinal damage.

[1] Orbital and adnexal injury have been shown to adversely affect the outcome of the open globe injuries [7, 15].

Intraocular Pressure (IOP) Assessment[2]

Hypotony strongly suggests an open-globe injury. However, normal or even high IOP does not exclude the presence of an open wound.

Slit Lamp Examination

- Examine the lids, conjunctiva, cornea, sclera, anterior chamber (AC), and lens in detail, and note the size and extent of the corneoscleral injury and associated injuries of the surrounding tissues.
- Determine if the corneal wound is self-sealing or not; perform Seidel test. After applying fluorescein dye (10%) topically, corneal wound is examined under blue light. Aqueous leak[3] dilutes the fluorescein dye, forming a green stream in the middle of the yellow dye originating from the wound, indicating that the wound is full thickness.
- If there is no obvious wound seen, look for signs of an occult scleral rupture such as hemorrhagic chemosis, asymmetric deepening of the anterior chamber, and low intraocular pressure (see Sect. 8.2.7.2).
- Conjunctival wounds must be thoroughly examined since they can obscure an underlying scleral wound or a subconjunctival foreign body.
- Examine vitreous and retina using slit lamp with a 90-diopter lens or indirect binocular ophthalmoscope[4] if the media is clear enough to allow visualization. Mydriatic use must be avoided in open-globe injuries with iris prolapse.

8.2.2 Imaging

In cases with hazy media, imaging studies are recommended to identify tissue injuries and presence of foreign bodies.

8.2.2.1 Computed Tomography (CT)

CT is the most often used radiological method in evaluation of ocular injuries, given that it provides reliable information about the injured eye as well as the orbit without leading to globe manipulation [16–18]:

- Orbital pathologies such as hemorrhage, abscess, and air and orbital and facial fractures
- Intraocular and intraorbital foreign bodies (see Sect. 8.3)
- Optic nerve damage and extraocular muscle damage
- Occult or posterior scleral wound
- Additional intraocular pathologies (e.g., lens damage, vitreous hemorrhage)

> **Tip:** A negative CT result does not necessarily mean that there is no pathology (e.g., an occult rupture or IOFB) present.
>
> In the presence of high clinical suspicion (regarding history and examination findings), exploratory surgery can be performed despite negative imaging tests.

> **Tip:** Common CT findings suggesting an open globe:
>
> - Irregular contour of the eyewall (Fig. 8.2)
> - Intraocular air
> - IOFB
> - Intraocular hemorrhage (Fig. 8.3)

8.2.2.2 Ultrasonography (USG)

In the hands of an experienced clinician, USG is able to demonstrate internal ocular anatomy more accurately than CT [16]. It can detect retinal detachment (Fig. 8.4), choroidal detachment, vit-

[2] Scleral indentation is contraindicated in the presence of an open globe.

[3] Scleral indentation is contraindicated in the presence of an open globe.

[4] Scleral indentation is contraindicated in the presence of an open globe.

Fig. 8.2 Open-globe injury. Axial non-contrast CT image demonstrates decreased volume and posterior contour irregularity of the right globe, consistent with the flat tire sign of open-globe injury, which indicates an unfavorable outcome

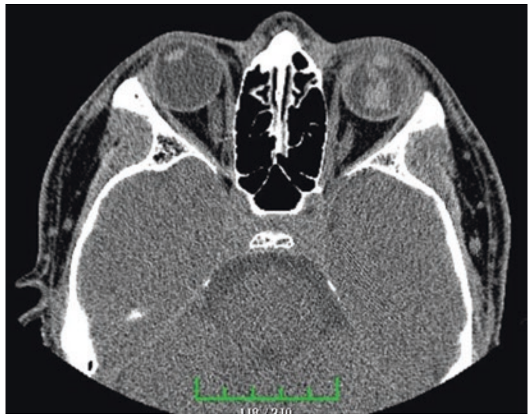

Fig. 8.3 Axial CT image demonstrates heterogeneous hyperdensity within the left vitreous body, consistent with vitreous hemorrhage. Note that despite uniform contour of the eyewall seen on CT, this patient actually had a penetrating injury in which prolapsed iris plugged the wound thus, to a certain degree, maintaining the tonus of the eye

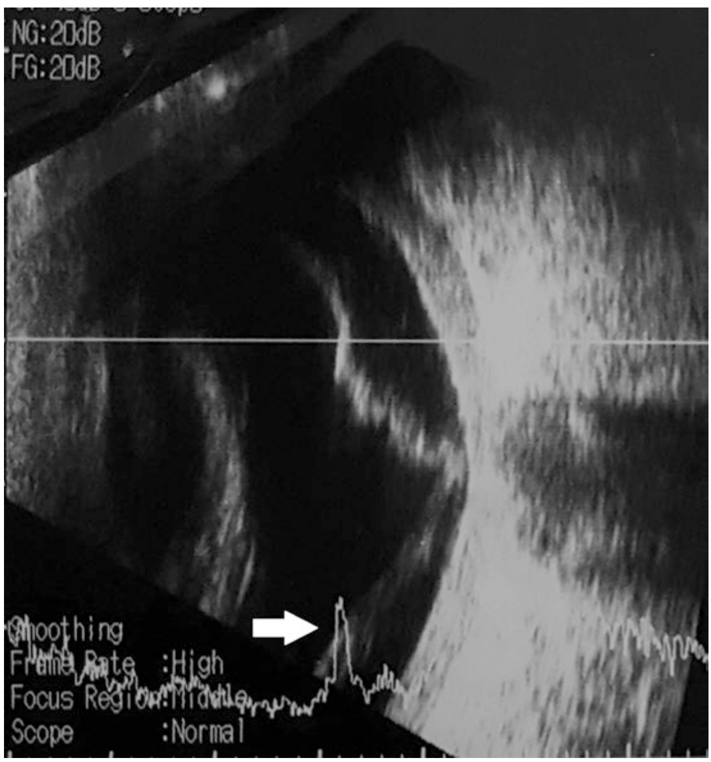

Fig. 8.4 B-scan USG of a patient with an assault-related injury demonstrates retinal detachment, confirmed with corresponding A-scan showing a high spike (arrow)

reous hemorrhage and opacities, posterior vitreous separation, as well as both radiolucent and radiopaque IOFBs in most of the cases, but its use is limited in open-globe injuries due to the necessity of globe manipulation.

> **Tip:** USG should be conducted with extreme caution in open globe injuries; alternatively, intraoperative use after wound closure can be attempted if there is a high risk of extrusion of ocular contents.

> **Tip:** Proper documentation of the findings obtained from the history and examination is critical both for clinical management and legal purposes.

8.2.3 Management of Open-Globe Injuries

Initial management of an open globe has mainly two purposes: prevention of expulsive choroidal hemorrhage (ECH) and prevention of endophthalmitis.

Key steps of the initial management are as follows:

- Place a rigid shield until surgery to protect the eye from any pressure that could cause further extrusion of intraocular contents. Patient should also be warned against touching the shield.
- Administer tetanus shots as necessary.
- Start endophthalmitis prophylaxis with intravenous antibiotics (see Sect. 8.4).
- Make sure the patient does not consume any food or fluids and begin preparation for general anesthesia and surgery.

8.2.4 Timing of Intervention

As a general rule, primary repair should be done as soon as possible [18, 19]. However, if appropriate equipment or operating staff is not available, delaying the surgery for a few hours is acceptable.

> **Tip:** If the risk of expulsive hemorrhage or endophthalmitis is very high, surgery is extremely urgent.

8.2.5 Staged vs. Comprehensive Primary Surgery

In the former approach, the primary surgery is limited to the wound closure, management of the prolapsed tissue, removal of any obvious foreign bodies located in the AC or at the wound lips, and irrigation of the hyphema as necessary. Thorough evaluation of the injury is carried out in the postoperative period, and a second surgery addressing the complicated pathologies can be planned in consultation with other colleagues.

On the other hand, in the latter approach, every co-existing pathology is addressed at the same time with the initial wound repair. This requires the ophthalmologist to be fully trained to work in the anterior as well as the posterior segment and have adequate experience in the trauma field.

Advantages and disadvantages of each approach are discussed in Table 8.3. Although there is an increasing trend toward performing comprehensive surgery in severe ocular injuries involving the posterior segment, the staged approach is definitely more practical and also the only option in many centers. Yet, controversy remains about the best timing of secondary intervention when the staged approach is adopted (see Sect. 8.2.8.5).

8.2.6 Primary Repair of Corneoscleral Wounds

Steps of the primary repair are as follows:

- Cleaning off the debris from the wound edges
- Dealing with prolapsed tissue
- Wound closure
- AC cleansing as necessary

> **Tip:** Repair of the adnexal injury should follow the repair of the globe itself because eyelid surgery can put pressure on an open globe.

8.2.6.1 Dealing with Prolapsed Tissue

Iris

Twenty-four hour of extrusion of iris was once accepted as deadline for the decision of excision [18, 23]. However, we now consider the condition of the iris as the determining factor rather than time.

Excision is only recommended for necrotic, nonviable (depigmented, macerated, feathery), and severely contaminated iris. Even in cases where excision is required, iris should be preserved as much as possible.

Repositioning İris is repositioned if it is viable, free from epithelial overgrowth and free from bacterial contamination. Prior to repositioning,

Table 8.3 Comparison of staged vs. comprehensive approach

	Staged approach	Comprehensive primary surgery
Advantages	Simple primary surgery, requiring less skill	Potential prevention of endophthalmitis by removing the inoculated media
	Availability of experienced surgical team and required equipment for secondary surgery	Early reduction of intraocular inflammation, thus prevention of PVR [21]
	Detailed evaluation of the extent of the injury can be carried out postoperatively	Early detection and treatment of possible retinal breaks or detachment
	Resolution of media opacities and spontaneous separation of posterior hyaloid face [20] make vitrectomy technically easier	Earlier visual rehabilitation
	Patients get used to and realize their condition better	
Disadvantages	Risk of endophthalmitis	Necessity of experienced surgical team and required equipment
	Increased PVR risk [21]	
		Risk of uncontrollable hemorrhage [20, 22]
		Risk of wound leakage during vitrectomy
		Increased vitreoretinal adhesions
		Visualization problems due to corneal edema
		Less accurate IOL power calculation
		Technically harder surgery
		May lead to the dissemination of a probable intraocular microorganism from anterior to posterior segment

epithelial cells debrided and possible organisms should be washed off the surface with topical antibiotics.

- For small prolapse, the use of miotics if it is entrapped in the periphery and mydriatics if it is in the central might be helpful.
- For corneal wounds, pulling of the tissue is more effective than pushing. A limbal paracentesis should be made at a convenient location where a spatula can be introduced for gentle sweeping. Once the iris is repositioned, viscoelastics or air can be injected to prevent reprolapse. This is also important to prevent postoperative synechia formation.
- For scleral wounds, gentle pushing of the tissue through the wound is the method for repositioning. The assistant may hold the iris back while the sclera is being sutured.
- Sometimes, careful dissection using forceps may be necessary if there is presence of fibrin or scar tissue (Fig. 8.5).

Choroid and Ciliary Body

Prolapsed choroid and ciliary body should always be repositioned since excision may cause severe complications such as intraoperative hemorrhage, postoperative inflammation, and phthisis. Diathermy may be performed gently to shrink the tissue for easier reposition.

Lens

Extruded lens triggers severe inflammation due to the release of antigenic lens proteins; hence any lens particles extruded or entrapped in the wound must be completely removed with the forceps before wound suturing.

Vitreous

Management is straightforward: Prolapsed vitreous through the wound or into the AC or into the lens must be totally excised since the remaining of it is related to serious complications such as retinal detachment [24, 25], chronic inflammation and cystoid macular edema, corneal decompensation, and hypotony [26].

> **Tip:** Preferred instrument for removal of vitreous is vitrectomy cutter, which also gives opportunity to clean the interior of the wound. Using sponges or scissors should be avoided which may exert tractional force on the retina causing retinal breaks and detachment.

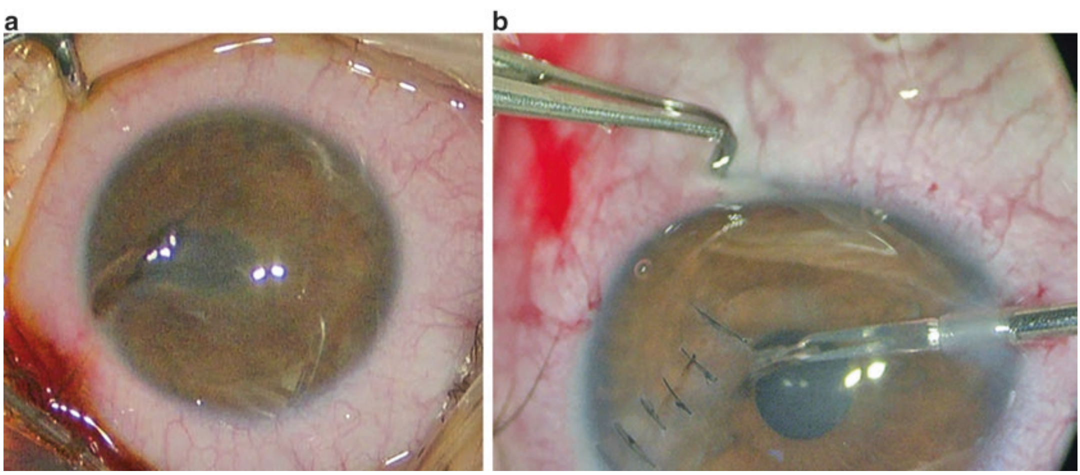

Fig. 8.5 Corneal laceration with prolapsed iris and peaked pupil (**a**). Fibrous tissue adherent to the iris which extends to the cornea was removed with forceps at the end of the surgery (**b**)

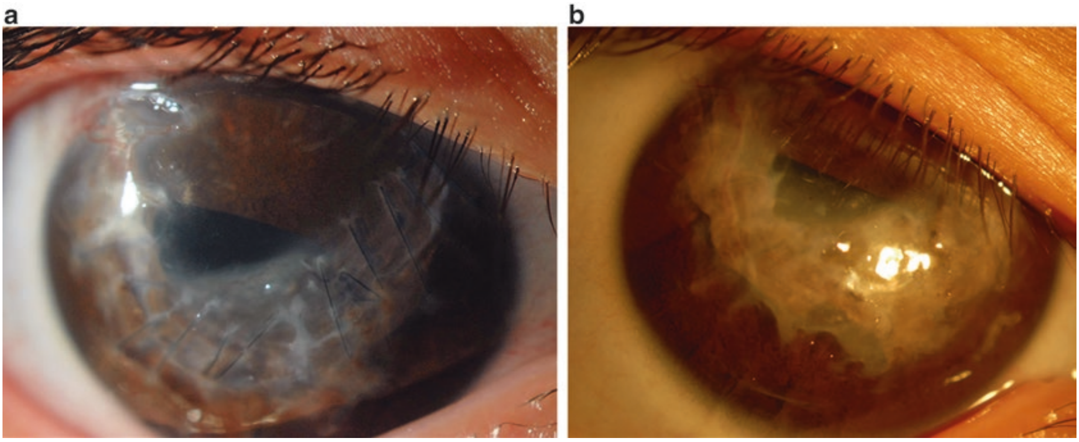

Fig. 8.6 Improperly closed corneal wound (left) had resulted in subsequent severe scar development with vascularization (right) in a 6-year-old boy which led to permanent visual impairment

It has been shown that the incidence of retinal detachment is higher if the wound is at ora serrata than at the equator because of the vitreous base (78% vs. 16%) [27]. Even though controversial, scleral buckling may be used for the wounds involving the vitreous base if vitreous removal is suboptimal and especially if secondary vitrectomy is less likely to be performed for any reason (see Sect. 8.2.8.4).

It is usually impossible to remove the vitreous completely in perforating injuries with very posteriorly located exit wounds. Posterior incarceration of the vitreous must be trimmed ab interno during vitrectomy in these cases.

> **Tip:** Recognition of prolapsed vitreous can be challenging in some cases. Triamcinolone may be used for staining of the vitreous fibrils. Pupillary deformation and vitreous strands directing toward the wound may be an indirect sign of vitreous presence in the AC.

Retina

Retinal prolapse is usually seen with large posterior ruptures, and it should always be repositioned. In cases of small prolapses, retina can be gently pushed back with the help of the viscoelastics while sutures through the sclera are being placed. However, it may be challenging to reposition it in cases of larger wounds where intraocular hemorrhage and/or high IOP causes extrusion. In these cases, repositioning should be attempted after the pathologies causing retinal extrusion has been dealt with.[5]

It is extremely important to excise all the vitreous adherent to the retina prior to repositioning. If retinal or vitreous incarceration occurs despite all attempts, subsequent PVR development is inevitable with poor prognosis [28, 29]. Early secondary vitreoretinal surgery is suggested along with aggressive anti-inflammatory therapy [30–32].

8.2.6.2 Wound Closure

While restoring the globe integrity is the main goal of the wound closure, minimizing corneal scarring and astigmatism with properly placed sutures is important as well for functional recovery in the postoperative period (Fig. 8.6).

Basic Principles of Corneal Wound Suturing

> **Tip:** Viscoelastic injection through a paracentesis provides AC formation as necessary during suturing. Another way to form the AC and stabilize the globe is to place initial temporary sutures which can be removed and replaced before the end of the case.

[5] Lowering the IOP and systemic blood pressure should be attempted.

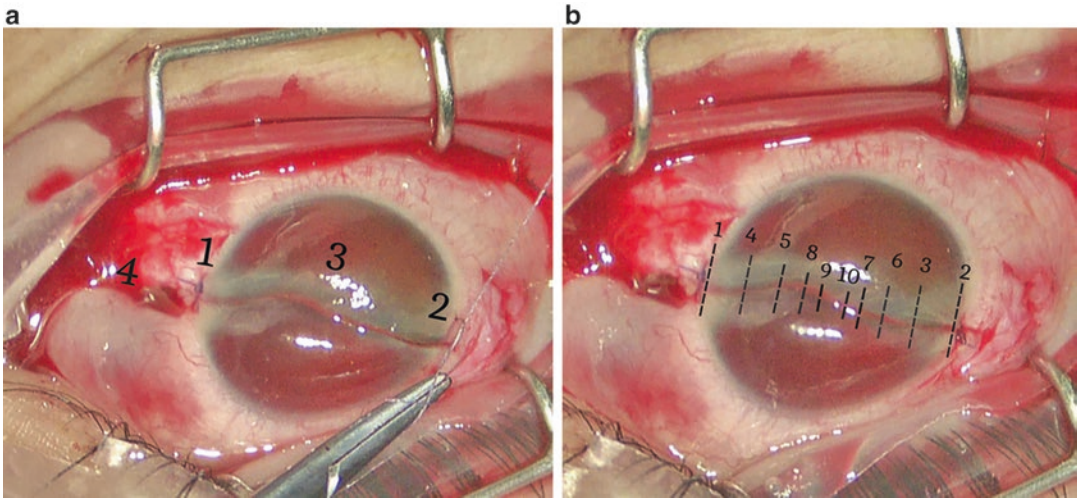

Fig. 8.7 If the wound crosses the limbus, the limbus is closed first, then the corneal part, and then the scleral part (**a**). Rowsey-Hays technique of corneal wound closure with long, tight, compressive suture bites at the periphery, with short, spaced, minimally compressive suture bites at the center to preserve corneal curvature as much as possible (**b**)

Order of Suture Placement

The first step when closing the eye is to identify where your landmarks (i.e., limbus and sharp angles of the wound) are and place the sutures these places first. This enables an anatomically correct repair, especially in large corneoscleral wounds where the integrity of the globe is severely disrupted.

- In cases of corneoscleral wounds, limbus should be closed first followed by the closure of the cornea and finally the closure of the sclera (Fig. 8.7a).
- If there is a limbus to limbus laceration, or similarly a long-wound crossing much of the cornea, suturing should start from the outsides and continue inward. The sutures within the central cornea should be shorter than those aligning the periphery to avoid flattening of the cornea in the center (Fig. 8.7b) [18, 33]. Ideally, no suture should be placed at the apex of the cornea.
- Otherwise, placing the first suture in the middle of the wound and continue suturing at 50% between the edge of the wound and the first suture is generally the method of choice.

Interrupted vs. Running Sutures

- Interrupted suturing with 10-0 or 11-0 nylon sutures with spatulated needles is the most preferred suturing method for the corneal wounds [16]. Interrupted sutures are placed perpendicular to the wound.
- Employing running sutures may fasten the procedure as well as provide continuous and uniform zone of compression [16]. However, they create a large zone of compression, thus excessive flattening of the cornea. The other disadvantage is that they induce wound slippage when they are introduced at 90° angle [34]. Hence, running sutures should only be used for long peripheral limbus-parallel wounds, with bites of it being introduced at 45° angle (Fig. 8.8). For all other situations, interrupted sutures should be used to avoid excessive flattening.

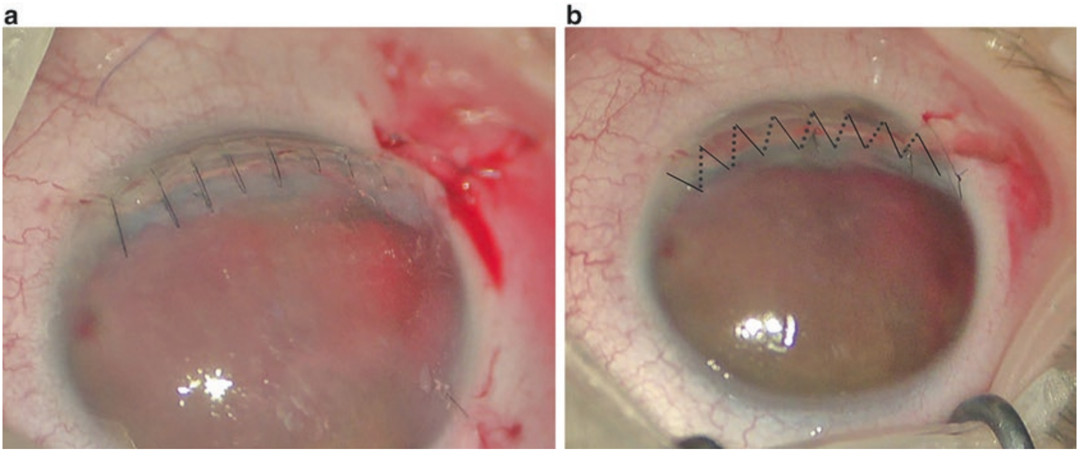

Fig. 8.8 Proper closure of a long peripheral limbus-parallel wound with interrupted sutures (**a**). A running suture could have been used alternatively in this peripheral wound, as illustrated (**b**)

- Interrupted sutures are also advantageous allowing manipulation of astigmatism with selective removal in the postoperative period.

Thickness: Partial vs. Full Thickness

Ideal suture depth is controversial. Traditional "90% depth" suture passing just over the Descemet's membrane has been suggested by many authors in an attempt to prevent introduction of the organisms into the eye [18, 35]. However, edematous wound edges in the acute setting of the trauma challenges layer to layer apposition with this technique. Because that tissue thickness differs due to the localized edema, you may end up with uneven suture depth on each side of the wound which would later cause tissue misalignment.

Conversely, Kuhn et al. suggested using of the full-thickness sutures as a solution to tissue misalignment due to uneven suture depth and corneal edema [34]. They proposed that even though full-thickness passage of the needle causes endothelial cell damage in that area, rapid blockage of the aqueous access to the stroma shortens the duration of the tissue edema. The risk of endophthalmitis, on the other hand, is not increased because the surrounding tissue edema creates compression enabling the rapid closure of the tunnel created between the extraocular space and AC. However, our approach is still traditional 90% depth suturing in regular wounds. If the wound is very irregular and the edges of the wound are very edematous, full-thickness sutures are preferred in our practice.

Bite Lengths

- Bites should be equidistant on each side from the wound margin for vertical lacerations.
- If one bite of the suture is longer than the other, the wound edge will likely override the other edge.
- In beveled lacerations, on the other hand, equal bite lengths should be created on the posterior surface of the wound creating a rectangular-shaped wound without any overriding or distortion [16].

> **Tip:** Do not forget to bury the knots at the end to avoid intense suture irritation postoperatively.

Wound Leakage

In cases of gaping, additional sutures or sutures with longer bites which have larger compression zones may be placed until a watertight closure is achieved. However, complex wounds such as stellate-shaped wounds are prone to leakage especially at the intersection points [18, 36]. And

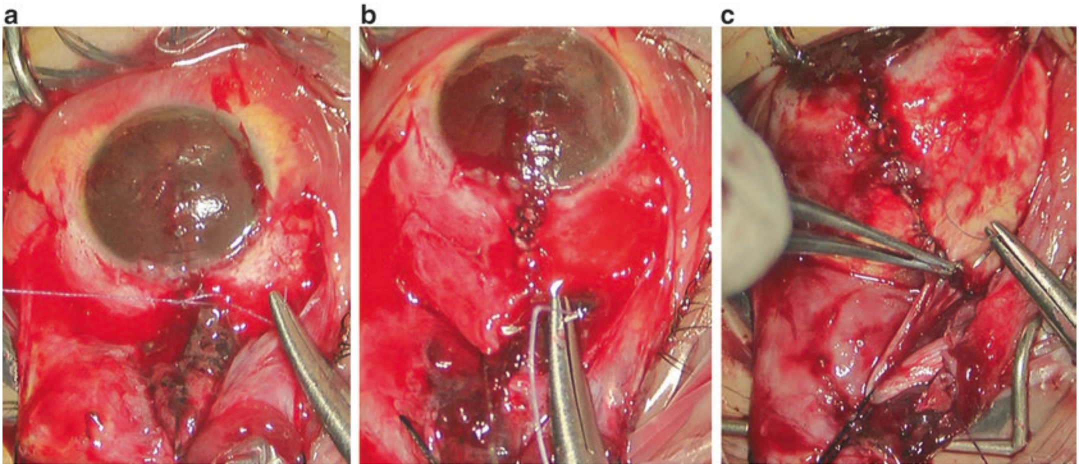

Fig. 8.9 "Close as you go" strategy for radial scleral wounds: Following closure of the corneal part of the wound, scleral sutures are introduced in an anteroposterior fashion. Once the eye has been stabilized, the peritomy is extended for further visualization of the wound. Retraction sutures through conjunctiva and Tenon's are used for optimal exposure (**a**, **b**). Since the wound goes beyond the insertion of the superior rectus muscle, it is retracted away with the help of a silk suture (**c**)

multiple suture passes through thin flaps of tissue may cause further leakage. In these cases, tissue glue (cyanoacrylate or fibrin) or bandage contact lenses may help in the sealing [37, 38]. In the setting of tissue loss, patch graft or tectonic PK may be required [35].

Basic Principles of Scleral Wound Suturing

- Scleral wounds are generally closed in an anteroposterior fashion, differently than corneal wounds.
- Prior to suturing, conjunctiva and Tenon's capsule must be completely cleared off the sclera, exposing the wound edges. Vitreous should be amputated at the wound edge and uveal tissues are repositioned. Sutures are introduced while scleral wound edges being grasped and raised with forceps. It is critical that an assistant holds the prolapsing tissues back with spatula to prevent tissue incarceration during suturing (zippering technique [39]).
- Interrupted sutures are used and 8/0 Vicryl sutures with a spatulated needle are generally preferred. However, nonabsorbable sutures (nylon, silk) may also be used according to the surgeon's preference. Around 80% suture depth is preferred to avoid choroidal hemorrhage and retinal injury.
- If a laceration involves the posterior sclera, open the conjunctiva a little, as you go, just enough to visualize next suture site in order to prevent deflating the eye (Fig. 8.9a, b).
- If the posterior scleral wound goes beyond the insertion of a rectus muscle, an assistant may gently retract the muscle with a hook or a suture for exposure (Fig. 8.9c). If this is not enough, muscle can be disinserted temporarily and reinserted after scleral defect is closed.
- Larger wounds with tissue loss or areas of scleral thinning (i.e., high myopia) may require patch grafting.

Tip: If wound is too posterior that closure requires too much pressure on the globe, thus risks tissue extrusion, it is better to leave it unsutured. Orbital soft tissue contents are usually able to exert enough pressure for the wound to close spontaneously, within few days postinjury.

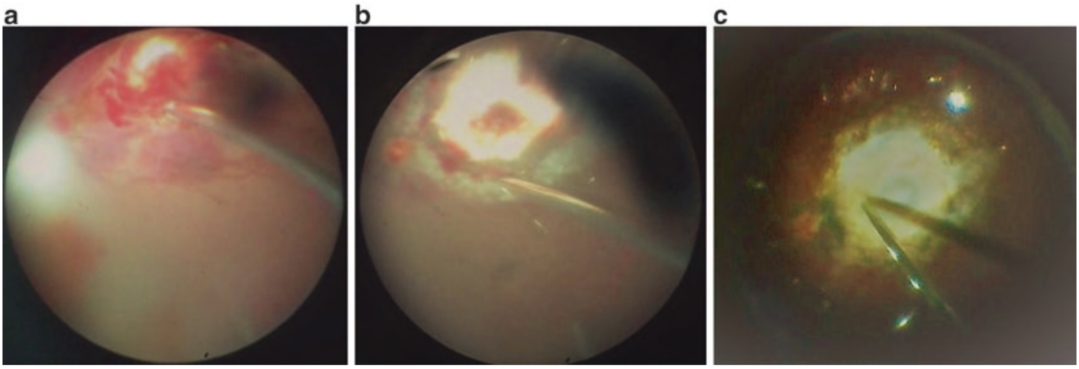

Fig. 8.10 A severe gunshot injury with an exit wound at the macula (**a**). This patient underwent prophylactic chorioretinectomy (**b**). No signs of PVR or retinal folds were observed during silicone oil removal, the bare sclera visible at the macular impact site, with RPE hypertrophy along the retinal edges (**c**). This case represents a good example of globe preservation with proactive treatment in severe cases

8.2.6.3 AC Cleansing as Necessary

- Hyphema causes AC inflammation and raised intraocular pressure.
- Irrigate out the hyphema, but do not try to remove the clot which can result with another vigorous hemorrhage. If a hyphema does occur intraoperatively, viscoelastics and an increased intraocular pressure can help stop the bleeding.
- Irrigate inflammatory and fibrinous debris as necessary.

8.2.7 Special Considerations in the Management of Different Types of Open-Globe Injuries

8.2.7.1 Lacerations (Penetrating and Perforating Injuries of the Eyeball)

Perforating ocular injuries are "through-and-through" globe defects with entry and exit sites. This is in contrast to penetrating injuries, which have a point of entry into the globe but no exit wound.

Penetrating injuries have somewhat better prognosis compared to ruptures and perforating injuries; the wound is usually smaller, and ECH risk is much lower [40]. However, the main problem with the penetrating injuries is the possible presence of an IOFB and high risk of endophthalmitis. Early recognition and proper management of these two issues are key to favorable outcomes with penetrating trauma (see Sects. 8.3 and 8.4).

Perforating injuries, on the other hand, differ in management and prognosis from penetrating injuries. They are more challenging due to the presence of an exit wound which is usually at an inaccessible location. It is important to distinguish if the injury is penetrating or perforating in order to prevent long-term complications. History of injury with long and sharp objects with a substantial momentum or injury with high speed missiles and gunshots suggest the possibility of an exit wound. Although the exit wound is usually smaller and the risk of retinal incarceration at the time of injury is less than ruptures, late scarring and PVR development is significant. Because of the threat of scar development, early secondary intervention with vitrectomy is necessary.

Kuhn and coworkers suggested prophylactic chorioretinectomy for treatment of perforating injuries against proliferative vitreoretinopathy [41]. Many authors, including us showed that this procedure is very effective in preventing both PVR and radiating retinal folds [42, 43]. We recommend early proactive surgery with prophylactic chorioretinectomy in perforating injuries in an attempt to decrease the PVR rates. We advocate this approach even in cases with macular impact site to augment retinal attachment and globe survival (Fig. 8.10).

Tip: Wound leakage may be a problem if the secondary intervention is during the first few days after the first intervention. Perfluorocarbon liquid leakage through the posterior exit wound is common. In such situations, it is wise to wait for a week before secondary intervention for the formation of some granulation tissue in the exit site, but it should not be longer than that which may induce severe PVR.

8.2.7.2 Ruptures

Ruptures have generally poorer prognosis than lacerations as severe intraocular damage occurs at the time of the impact and subsequent scar formation causes further damage. Therefore, recognition of a rupture and proper management are critical in prognosis.

A ruptured globe with a disrupted integrity and extruding contents is easy to recognize. However, a rupture may also be fairly subtle, so you need to check for other clinical signs that suggests an occult rupture:

- History of trauma caused by large, blunt object with substantial momentum
- Poor initial VA (LP or NLP)
- Low IOP (<10 mmHg)
- Thick subconjunctival hemorrhage (often 360°) and chemosis (Fig. 8.11)
- Peaked pupil and anterior vitreous strands in the AC (directing toward the wound)
- Asymmetric AC depth usually with hyphema
- Loss of the iris/lens/IOL

Ruptures typically occur at the sites of greatest structural weakness which may or may not be at the impact site, near the equator and directly behind the insertion of the rectus muscles, at the limbus, or at the site of previous intraocular surgery.[6]

Keys to the Management of Ruptures

- Primary wound closure should be performed as soon as possible since the ECH risk is high in cases of ruptures.
- A 360° peritomy may be necessary to uncover an occult rupture or multiple ruptures are suspected.
- “Close as you go” procedure can be used for radial and posteriorly extending scleral wounds to avoid further tissue prolapse. Very posterior wounds where the forceful closure will exert pressure on the globe should be left unsutured.

Tip: Occult and multiple ruptures may be present, all of which should be identified with careful investigation during surgery.

Vitreous incarceration is almost inevitable in most of the cases with posterior scleral ruptures (zone III injuries), and even retinal incarceration may occur despite all efforts. Primary comprehensive surgery or early vitrectomy should be considered in these cases to prevent subsequent retinal detachment and PVR development. Prophylactic chorioretinectomy should also be considered. However, it should be kept in mind that early vitrectomy in an eye with an unsutured wound poses the risk of reopening of the wound with extrusion of the retina.

8.2.8 Controversies Regarding Management

8.2.8.1 Primary Lens Extraction and Intraocular Lens Implantation

Extraction of an injured lens at the time of primary wound repair has distinct advantages such as controlling of inflammation and intraocular pressure [44, 45], direct visualization of the posterior segment, rapid visual recovery [46, 47] with prevention of deprivation amblyopia in pediatric population, and preventing development of anterior PVR in cases of lens-vitreous admixture [48].

[6] Determine whether refractive or open globe surgery (PK, ECCE) had ever been performed on the cornea if a blunt object caused the injury.

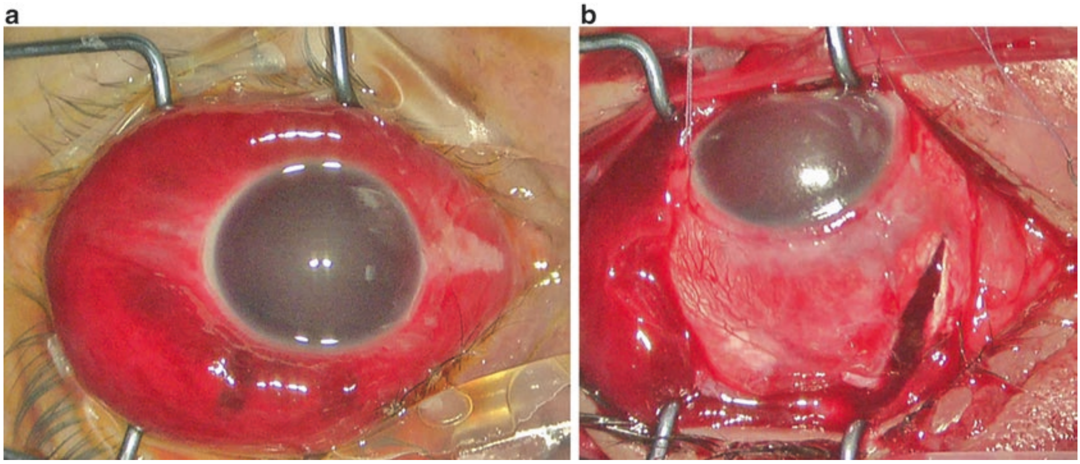

Fig. 8.11 Thick subconjunctival hemorrhage, especially if chemosis accompanies (**a**), should raise suspicion of an occult rupture (**b**)

However, the injury is rarely limited to the lens alone, and the extent of the lens disruption and possible associated injuries of the zonules, posterior capsule, and posterior segment may be very difficult to assess at the time of the injury, in the presence of blood, fibrin, debris in the AC, and cloudy cornea. It may be better to leave the injured lens alone at the time of the open-globe repair rather than performing a compromised surgery because of the lack of expertise or infrastructure facility. Such cases can be addressed later by an experienced posterior segment surgeon, under a controlled situation,[7] preferably after the capsule has fibrosed and stabilized. Nonetheless, in cases of significant anterior capsule disruption with free-floating lens material in the AC and where vitreous admixed in the ruptured lens, only these free floating lens particles may be removed during the primary repair; early secondary surgery in few days is warranted to prevent complications and PVR development.

The other controversy in this matter is whether an intraocular lens (IOL) should be implanted concurrently with the cataract removal or not during primary repair. Primary implantation of an IOL allows timely visual rehabilitation [46, 49, 50], which is crucially important in patients in the amblyopic age. On the other hand, it may be difficult, if not impossible, to determine the correct IOL power preoperatively; the inflammatory debris can settle on the IOL surface, requiring postoperative YAG capsulotomy or even surgery; it causes additional source of inflammation; the edge of the IOL may interfere with the visualization should subsequent PVR development necessitate vitrectomy [45]. Given the excellent outcomes seen with secondary lens implantation [51] and the substantial risk of endophthalmitis [52, 53], potential retinal complications in traumatized eyes, and severe inflammatory debris which may settle on the IOL, our general approach is to defer IOL implantation in the acute setting of an open-globe injury.

8.2.8.2 Vitreous Tap and Intravitreal Administration of Antibiotics

Routine use of intravitreal antibiotics is controversial and not widely accepted in the absence of manifest endophthalmitis [24, 52]. There is always risk of associated choroidal or retinal detachment in the setting of an open globe; thus, blind injections may pose additional risk of injection going inadvertently into the subretinal or

[7] Ophthalmologist should have been applying judicious topical corticosteroid therapy after the primary wound closure to control the postoperative inflammation, along with the antiglaucoma medication and topical antibiotics.

suprachoroidal space. Hence, vitreous tap and subsequent intravitreal antibiotic administration is recommended only if there are clinical signs of infection or in the presence of high-risk injuries [54, 55], organic IOFB, soil contamination, rural setting (Fig. 8.12), and delayed primary closure of the wound (see Sect. 8.4 for details).

8.2.8.3 Role of Prophylactic Cryotherapy

It has been shown that cryotherapy causes extensive breakdown of the blood-retinal barrier with intravitreal dispersion of RPE cells, which is known to lead to the increased inflammation and subsequent development of proliferative vitreoretinopathy [56, 57]. Campochiaro et al. showed that cryotherapy triggered the formation of a traction retinal detachment in a model of scleral laceration in rabbits [58]. Therefore, prophylactic barrage laser photocoagulation is preferred in cases of a retinal pathology that requires treatment.

8.2.8.4 Role of Prophylactic Buckle

Prophylactic scleral buckling theoretically would tamponade undetected retinal tears and minimize vitreous traction, preventing late retinal detachments. However, the literature remains divided whether a scleral buckle actually decrease the subsequent risk of retinal detachment or not; several studies have shown the benefit of placing a prophylactic scleral buckle [59–62] in the setting of an open-globe injury while others have not [63].

Nevertheless, if the wound extends posterior to the ora serrata and the peripheral retina cannot be visualized, or if there is retinal incarceration, prophylactic scleral buckle should be considered [61, 64].

> **Tip:** If the surgeon decides to place a prophylactic buckle, this is ideally done during the primary repair, because the development of subconjunctival scarring a few days later makes the placement difficult.

8.2.8.5 Timing of Secondary Reconstruction with Vitrectomy

When the surgeon adopts a staged approach in the management of an open-globe injury, the timing of vitrectomy still remains a topic of considerable debate [24, 65, 66].

Although early vitrectomy (at days 1–4) promises a decrease in PVR rates by prevention of early fibroblastic activity [21, 67], it is technically more difficult because of the increased incidence of vitreoretinal adhesions, corneal edema precluding visualization, leakage from the laceration area, and risk of uncontrollable hemorrhage due to uveal congestion [24]. Because of these difficulties, many surgeons prefer the surgery after this acute period but sooner than 2 weeks after trauma, with reported favorable outcomes [22, 61]. However, deferring vitrectomy more than 2 weeks has severe disadvantages, like PVR, ciliary body destruction, and consequent phthisis [31], hence is not recommended.

Our approach is to perform immediate surgery in cases of traumatic endophthalmitis and as soon as possible (within days) surgery in eyes with IOFB with a high risk of infection. It is also wise to perform vitrectomy within days in eyes with a mixture of lens fragments and vitreous in anterior chamber and in eyes with zone III lacerations where a retinal break is definite. Eyes with dense vitreous hemorrhage may be operated relatively earlier to uncover possible retinal tears or detachment [68] and to prevent late tractional retinal detachment and PVR which is expected to occur more rapidly than usual in the setting of a hemorrhage [31, 69]. Otherwise, we generally perform vitrectomy approximately 5–10 days postinjury to allow media clarity, wound stabilization, and posterior vitreous detachment to set in. We do not recommend delaying the surgery any longer than 10 days as any further delay can result in significant PVR.

8.2.8.6 Reconstruction vs. Primary Enucleation in Eyes with No Light Perception

All open globes should be repaired initially, unless there is a profound loss of intraocular con-

Fig. 8.12 An 18-year-old male presented 12 h after sustaining a penetrating injury by a chisel while cutting wood in a farm house. Orbital CT showed no IOFB. He had zone II injury with iris and vitreous prolapsus (**a**). Oral moxifloxacin treatment was started as infection prophylaxis, and he underwent immediate primary wound closure (**b**). Postoperative USG yielded attached retina, and he was discharged the next day, with medication of oral moxifloxacin and topical antibiotic, steroid, and cycloplegic. Since the lens was injured and the fragmented badly, a secondary surgery was planned within a week. However, he presented with severe pain and upper lid edema, proptosis, limited range of ocular movements, and hemorrhagic discharge the next week (**c**, **d**). He was diagnosed as panophthalmitis and broad-spectrum antibiotics (ceftazidime, teicoplanin—he was allergic to vancomycin) administered intravenously. Signs of infection partially subsided within several days, with the presence of scleromalacia at the superior sclera (**e**). However, elevated liver enzymes due to systemic antibiotic treatment, inadequate response to treatment, and threat of sympathetic ophthalmia (photophobia and blurry vision of the fellow eye) justified enucleation in this patient. This case may demonstrate the importance of intravitreal antibiotics and/or close observation in the management of an injury in rural setting, with possible soil contamination

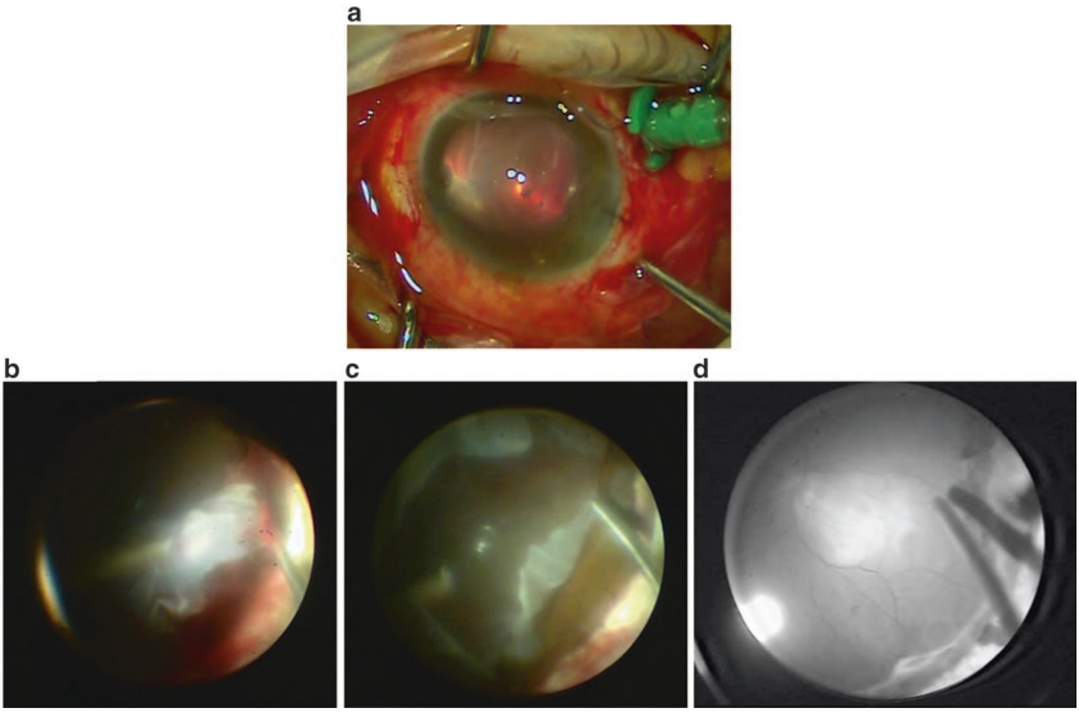

Fig. 8.13 A case of reversible NLP status. A 58-year-old female with zone III penetrating injury referred to us after primary repair elsewhere. She had NLP vision with hyphema and preoperative USG yielded retinal detachment with dense subretinal and vitreous hemorrhage. She underwent surgery 7 days after primary injury. Following phacoemulsification + IOL implantation (**a**), the dense vitreous hemorrhage was started to dig from the nasal side till reaching the retina. This step is important to avoid further retinal damage. When the retina was reached, it was very difficult to detach hemorrhagic vitreous from the detached retina. There was 180 degrees of primary laceration parallel to the limbus in the superotemporal post-equatorial area where retinal incarceration and huge subretinal hematoma was present (**b**). Ciliary body was also damaged in this laceration area. A 360 retinotomy and peripheral retinectomy was performed to clear the subretinal dense coagulum, retinal incarceration was relieved (**c**), and 360 peripheral laser with silicone oil tamponade resulted in retinal reattachment. Figure (**d**) shows the attached retina during silicone oil removal surgery. Retina remained attached, intraocular pressure was around 8 mmHg (because of ciliary body damage in the laceration area), and visual acuity improved to 20/100 during 12 months of follow-up examination

tents which makes anatomic reconstruction impossible. The idea of potentially losing an eye is a devastating situation to which the patient needs time to adjust. In addition, no light perception (NLP) at the acute setting does not necessarily mean that this is irreversible. It has been shown that visual recovery rates from NLP to LP or better after open-globe injuries range from 4% to 33% [70–72].

Visual acuity can be profoundly impaired to the extent of NLP due to treatable pathologies (e.g., severe corneal edema, hyphema, dense vitreous and subretinal hemorrhage, retinal detachment, extensive choroidal hemorrhage), correction of which may reverse NLP status (Fig. 8.13).

Only in cases of optic nerve transection or complete avulsion, the ophthalmologist may be certain that NLP status is permanent (Fig. 8.14). Even in these cases with no visual potential, the aim should be the anatomic salvage of the globe.

Traditionally, primary enucleation had been advocated for severely traumatized eyes with NLP in view of the risk of sympathetic ophthalmia [73, 74]. However, this approach is no longer recommended as modern immunosuppressives improved the control and treatment of sympathetic ophthalmia [75] and the reported rates of

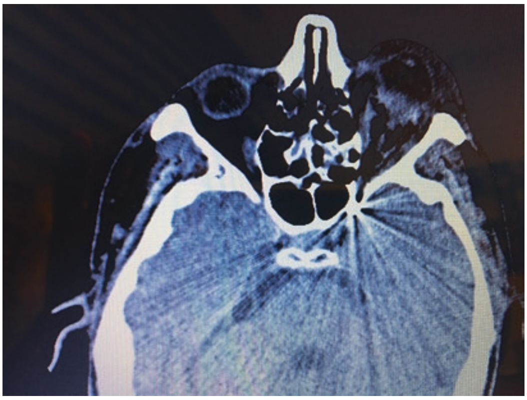

Fig. 8.14 NLP eye with a foreign body in orbital apex. Optic nerve trauma is the cause of lost LP

sympathetic ophthalmia is very low in recent studies [76, 77]. Currently, we recommend globe salvaging procedures for eyes with severe trauma with NLP vision at the initial presentation. Secondary enucleation is mostly carried out for blind painful eyes in our practice.

8.3 Intraocular Foreign Bodies

8.3.1 Introduction

Intraocular foreign bodies (IOFB) are a particularly important subset of ocular trauma, in association with 18–41% of all open-globe injuries [78–80]. An IOFB is technically a penetrating injury but is grouped separately because of different clinical implications; besides damage occurring at the time of the initial injury, associated conditions such as endophthalmitis, late metallosis, and subsequent scarring (i.e., PVR) significantly affect visual prognosis.

The most common causes include hammering (60–80%) [81, 82], usage of power or machine tools (18–25%), and weapon-related injuries (19%) [80], which typically affect young males mostly.

8.3.2 Pathophysiology

IOFBs cause damage in several ways:

- Direct mechanical damage
- Chemical damage (metallosis)
- Other complications (i.e., endophthalmitis, PVR; will be discussed later)

8.3.2.1 Direct Mechanical Damage

- The majority of the IOFBs are found in the posterior segment (58–88%), with most others in the anterior chamber (10–15%) or the lens (2–8%) [83]. A posterior segment IOFB has a 68% risk of causing a retinal lesion [80].
- IOFBs that penetrate through the sclera preserve more energy compared to those entering through the cornea [84], hence have a higher risk of causing a perforating injury.
- The length of the entry wound is closely related to the risk of retinal damage: the shorter the wound, the less energy to be lost during penetration; hence, more damage is caused [80].

8.3.2.2 Metallosis

By far, most IOFBs are metallic in nature [85] which pose a risk for chemical toxicity (Table 8.4).

8.3.3 Diagnosis

8.3.3.1 History

A reliable history emphasizing on the mechanism of injury and the setting in which the injury occurred might help identify the presence of an IOFB and its nature (metallic vs. vegetate) and location.

In cases of explosion and war injuries, the clinician should be aware that multiple IOFBs may be present [87].

Table 8.4 Long-term toxicosis

Chalcosis (due to copper content)[a]	Siderosis (due to iron content)[b]
Deteriorating visual acuity	Brownish deposits on the corneal endothelium
Kayser – Fleischer ring	Brownish discoloration of the iris (heterochromia)
Sunflower cataract	Chronic open-angle glaucoma
Greenish discoloration of the iris	Dilated, nonreactive pupil
Chronic uveitis	Yellowish cataract with brown capsular deposits
Glaucoma	Pigmentary degeneration of the retina
Vitreous opacities	Optic disk hyperemia, edema
ERG changes	ERG changes

[a]Pure copper IOFBs may rapidly cause intense inflammatory response with melting, hypopyon, and retinal detachment, mimicking endophthalmitis, which may result in acute loss of vision, eventually phthisis [86]. Once the threat of acute reaction has passed, a copper IOFB can remain silent for years

[b]Development of siderosis, on the other hand, has somewhat slower onset [80]

Tip: Approximately 20% of the patients do not experience pain or visual change [80], with some of them being unaware of an object entering their eyes. The clinician should always be suspicious of a potential IOFB(s) in the setting of an open-globe injury despite a negative history.

8.3.3.2 Clinical Presentations and Signs

Apart from symptoms and signs of an open globe (pain, reduced visual acuity, decreased IOP, shallow AC, pupillary distortion toward the penetration site), some direct or indirect signs might indicate an IOFB:

- Wound track, localized corneal edema, focal lens opacities, rupture of the lens capsule, and nonsurgical hole in the iris may provide trajectory information implying the presence and likely location of an IOFB.
- Another clue that might suggest an occult IOFB may be an eye with endophthalmitis which does not respond to proper antibiotic therapy [52].

Ophthalmoscopy provides information about the location of IOFB as well as associated ocular injury in most of the eyes with clear media. However, for the IOFBs stuck in the angle or located very anteriorly in the posterior segment, gonioscopy and scleral indentation are needed which can only be used after wound closure.

In cases with hazy media where IOFB cannot be visualized, imaging techniques are required.

8.3.4 Imaging

8.3.4.1 Plain X-Ray

In the current practice, X-ray has been replaced by CT as the primary diagnostic tool as CT has become widely available and more than half of the nonmetallic foreign bodies may be missed by X-ray [88].

8.3.4.2 Computed Tomography (CT)

CT without contrast is the first-line diagnostic modality for evaluating the injured eye, with a sensitivity of detection of 100% of IOFBs >0.06 mm^3 and 45–65% for IOFBs <0.06 mm^3 [80]. Scanning in both axial and coronal planes with thin cuts (1.0–1.5 mm) is required.

Helical CT over conventional CT may provide even higher sensitivity with better multiplanar reconstruction ability and reduced motion artifacts [89, 90].

However, ceramic, plastic [91], and even metallic IOFBs [92] may be missed, especially if too wide cuts are utilized. Wooden foreign bodies may resemble air, appearing hypodense on CT which may cause false-negative results. Geometric shape of the IOFB (oblong/elongated) may aid in the differentiation.

8.3.4.3 Ultrasonography (USG)

In the hands of a skilled clinician, ultrasound is extremely helpful in detecting accurate location of IOFBs, even nonmetallic ones. Especially when the object is closest to the eyewall, it may be difficult with CT scan to identify whether it is intra- or extraocular due to reflection artifact. USG may provide more accurate assessment in this matter as well as extent of associated tissue injuries [16, 83].

It may be used with extreme caution even if the globe is still open; alternatively, intraoperative use after wound closure can be attempted.

Appearance of IOFBs may be intraocular strong echoes with posterior acoustic shadowing (Fig. 8.20c). An air bubble in the vitreous can resemble this appearance with ultrasonography, causing a false-positive result [93]. Conversely, wood and vegetable matter may resemble blood or vitritis, causing false-negative results [83].

8.3.4.4 Ultrasound Biomicroscopy

This test may be the sole method of detecting the presence of small nonmetallic IOFBs located at the anterior segment (e.g., angle, ciliary body). However, it is not recommended if the injury is open globe.

8.3.4.5 Magnetic Resonance Imaging (MRI)

MRI is not recommended unless the presence of a metallic foreign body is ruled out.

8.3.5 Management

The initial management of the injury follows the steps described in Sect. 8.2 (e.g., anti-infection, anti-tetanus therapies, emergency surgery).

8.3.5.1 Timing of IOFB Removal

General rule is the removal of all fresh IOFBs as early as possible because of the potential risk of endophthalmitis and toxicity [94, 95]. However, optimal timing of IOFB removal is controversial [96, 97].

Delayed IOFB removal has potential advantages such as improved control of inflammation, resolution of media opacities [98], and the possible development of posterior hyaloid detachment [24] which is critical for the surgery. Nevertheless, removal of the IOFB during primary surgery should probably be pursued in the presence of an experienced surgeon and operating staff, especially if there is posterior segment or a high-risk injury. An individual decision must be made regarding the factors outlined in Table 8.5.

> **Tip:** Incidentally found, symptomless chronic IOFBs should be removed if there are signs of metallosis (e.g., ERG changes), if mechanical damage threatens (e.g., sharp glass particle in the vitreous) or based on the patients' desire (e.g., inconvenience for follow-up). Otherwise they can be closely monitored with thorough ocular examinations and serial ERGs.

Table 8.5 Factors influencing the timing of IOFB removal

Immediate	Delayed[a]
Endophthalmitis upon presentation[b]	Presence of life-threatening injuries
High risk of endophthalmitis[b]	Less experienced surgeon and unavailability of necessary equipment[c]
(e.g., organic IOFB, soil contamination, rural setting, lens injury)	Perforating injury[d]
Presence of copper	
Risk of retinal injury[e]	

[a]IOFB removal should not be delayed more than 10 days; a few weeks will increase almost fourfold the risk of proliferation and tractional retinal detachment [31]

[b]Intravitreal antibiotics should be considered along with IOFB removal

[c]If the surgeon is not experienced for comprehensive surgery, deferred IOFB removal and temporization with primary globe closure and administration of systemic and intravitreal antibiotics is reasonable

[d]If there is a posterior exit wound, waiting for several days should be considered to avoid spontaneous opening of the wound

[e]In cases involving retinal break or detachment, the surgery becomes more urgent. If media opacity obscures the retinal view, indirect clues such as wound length and location may be used for prediction of retinal impact

8.3.5.2 Instrumentation

Intraocular forceps and magnets can be used for IOFB removal. There are two types of magnets: external electromagnets (EEM) and intraocular rare earth magnets (IOM). EEM has strong pull force, but it can only be used outside the eye which causes free-flying of the IOFB beyond the surgeon's control. On the other hand, IOM creates a unidirectional force which is exerted at a close proximity to the IOFB with fine control. IOM allows easier engagement than an intraocular forceps which requires dexterity to grasp the IOFB. However, other than small foreign bodies (<3 mm), IOFBs often get caught in the wound during extraction with the magnet alone, which requires additional forceps use [95].

8.3.5.3 Surgical Steps

The appropriate surgical technique for IOFB removal depends on the location and composition of the IOFB.

Anterior Chamber

Anterior chamber IOFBs are generally removed during primary surgery. However, removal of IOFBs through the entrance wound is generally not recommended due to the potential further tissue damage.

- Unless there is a large object stuck in the angle or iris, the original wound should be closed first, and then a new paracentesis should be created for extraction at a convenient location, preferably 90–180 degrees away from the IOFB for the ease of manipulations.
- Viscoelastics should be used to maintain chamber depth and protect the endothelium and lens integrity before attempting removal.
- Inducing miosis may be helpful to protect the lens and bring the IOFB (lying on or embedded in the iris) to a more central position.
- Intraocular magnets or forceps may be used for extraction, based on the composition.

Lens

The IOFB and the lens may be left in situ, typically in cases such as:

- Inert objects (nonmetallic, nonorganic) that embed themselves in the lens
- Capsular breach less than 2 mm (which usually heals without leading to cataract)

Nonetheless, it should be kept in mind that encapsulation of IOFB by the lens does not necessarily eliminate the risk of siderosis [99]. Close observation of the patient serial electroretinograms for any signs of complications is warranted in the cases of deferred removal of metallic IOFBs.

Otherwise, intralenticular IOFB extraction is generally performed concomitantly with cataract removal. If the lens is to be removed, different surgical techniques (phacoemulsification, ECCE, ICCE, vitrectomy) may be preferred, determined by the presence of posterior capsular injury and vitreous prolapse. IOL placement should be deferred when vitreoretinal damage is suspected or endophthalmitis is present or is at high risk of developing [52].

> **Tip:** If there is a high risk of anterior PVR development, both anterior and posterior lens capsules should be removed in an attempt to prevent it to become "scaffold" for proliferation.

Posterior Segment

Most of the posterior segment IOFBs are removed by pars plana vitrectomy, which also enables vitreous sampling, clearance of the media opacities, and treatment of associated tissue damage in conjunction with IOFB removal [100].

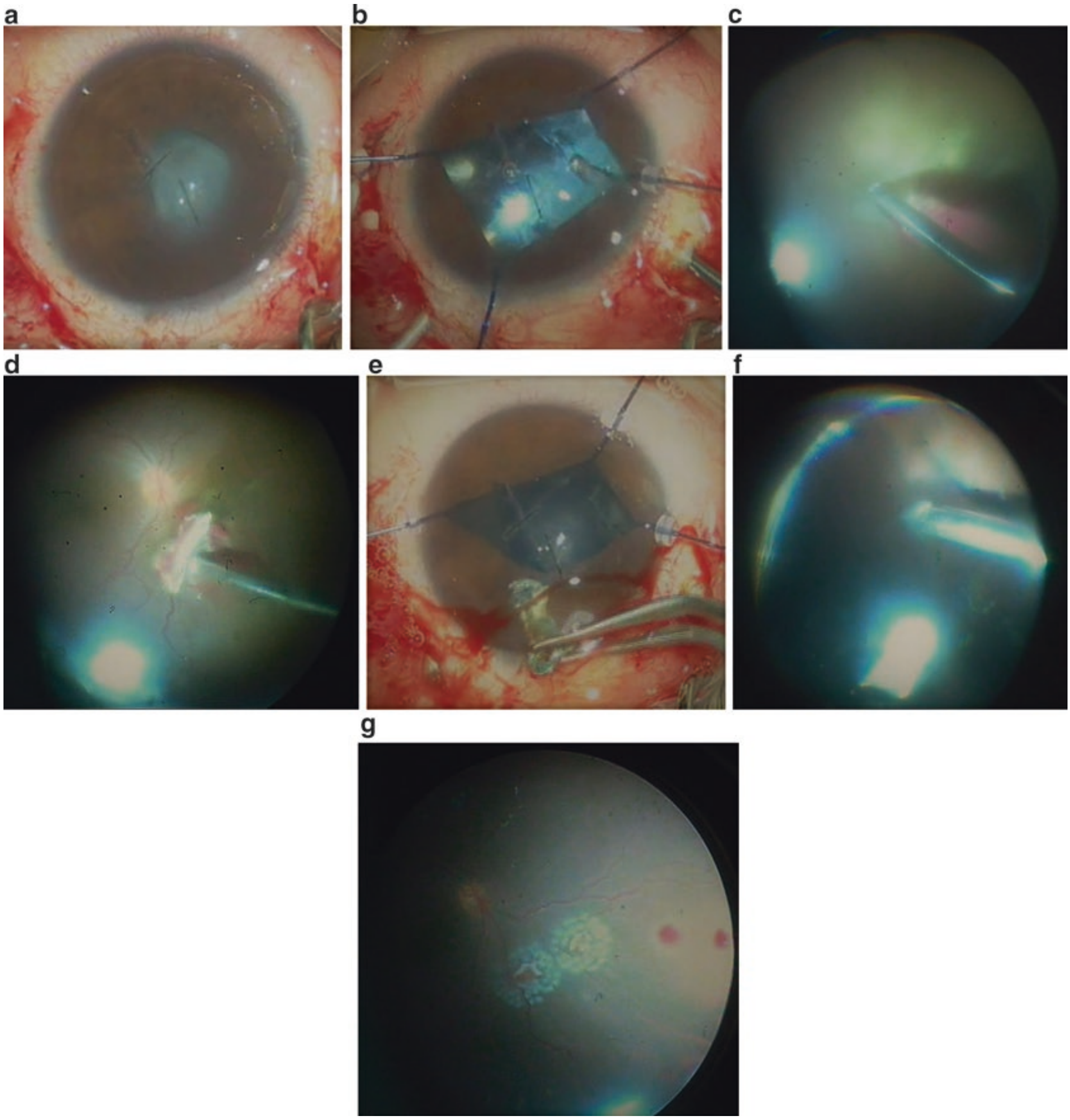

Fig. 8.15 A 9-year-old girl presented with traumatic cataract and IOFB after a pellet gun injury (**a**). Pars plana lensectomy was performed with the use of iris retractors (**b**). Vitreous opacities and posterior hyaloid were removed (**c**). After reaching the IOFB, it was fully freed by removing any adherent vitreous strands (**d**). Then it was transferred to the AC with passive aspiration and extracted via limbal route with the help of viscoelastics (**e**). Later, vitreous removal completed at the base, and peripheral retina was checked to detect any tears (**f**). Tears at the impact site surrounded by endolaser, along with 360 degrees of peripheral retina (**g**). Gas tamponade used at the end of the surgery

Steps of IOFB removal by vitrectomy as follows (Fig. 8.15):

- Media opacities (e.g., hyphema, cataract, vitreous hemorrhage) should be removed prior to removal of the posterior segment IOFB.
- Infusion port should be entered and used only after one can verify the location of the tip of the infusion in the vitreous cavity.
- Remove vitreous as much as needed until the intravitreal IOFB is reached or remove completely in the cases of retinal IOFB.

- The IOFB should then be fully freed by removing any adherent vitreous strands. Use a sharp instrument (e.g., MVR blade, scissors) to break all its connections from the retina and/or to open the encapsulating fibrous tissue if necessary.
- Estimate the size of the IOFB by comparing it with optic disk or vitrectomy probe, and prepare the extraction site slightly larger than that.

Tip: In the cases where retinal detachment is present, infusion of a perfluorocarbon can partially or fully reattach the retina, making IOFB extraction safer and more efficient.

– Pars plana delivery, through enlarged sclerotomy, usually suffices [97].
– For larger IOFBs whose total volume is greater than $4.0 \times 4.0 \times 4.0$ mm^3, making an "L"- or "T"-shaped sclerotomy should be considered instead of a long linear incision [83].
– For very large IOFBs, limbal delivery after transferring the IOFB into the anterior chamber by transpupillary route is recommended [95]. The drawback of this method is that it may induce postoperative corneal astigmatism and incision-related problems [101].

- Align the IOFB to make the thinnest part be removed through the port site first. Open the wound with tooth forceps, and slowly remove the IOFB with forceps or intraocular rare earth magnet in selected cases (i.e., small IOFB).
- Complete the vitrectomy.
- Do laser prophylaxis to retinal impact sites (if the IOFB is impacted in the retina, the surrounding laser is recommended before removal).
- Examine the retina completely with scleral depression and check for retinal tears, retinal detachment or choroidal detachment.
- The posterior hyaloid should be removed to reduce the risk for postoperative epiretinal membrane formation with subsequent risk of postoperative retinal detachment [102]. However, in the presence of severe intraocular inflammation with areas of retinitis where retina seems fragile, posterior hyaloid removal may be deferred in order to avoid retinal break formation. This may be later addressed at a planned secondary vitrectomy, by the time spontaneous posterior vitreous detachment most likely will have occurred.
- Consider endolaser cerclage or scleral buckle.
- Prophylactic buckling theoretically decreases vitreous traction indirectly and prevent retinal detachment from potential retinal breaks. However, whether it is beneficial or not remains controversial [60] (discussed in Sect. 8.2).
- Endolaser cerclage is another option which technically creates a new ora serrata, covering the area where retinal breaks are likely to develop. It may also play a role in the prevention of PVR by destroying tissue that may be responsible for the release of inciting agents [102].

Alternative techniques to vitrectomy:

- Rarely, if a small IOFB is suspended in the vitreous without causing any significant
- posterior segment pathology, it may be removed with an IOM or a forceps without performing vitrectomy (Fig. 8.16). However, a complete vitrectomy is needed if there is

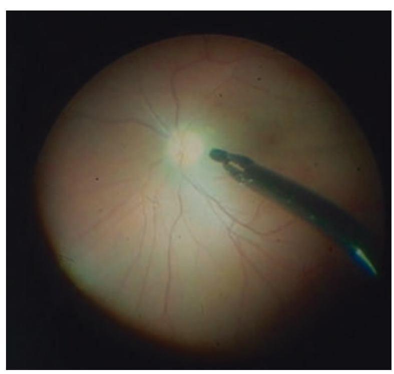

Fig. 8.16 An IOFB suspended in the vitreous is removed by forceps without the need for vitrectomy

vitreous hemorrhage or a retinal lesion as well as in the case of vitreous incarceration in the wound.

- IOFB in the peripheral retina may be removed by external magnet with scleral cutdown if there is no vitreous incarceration in the wound. However, this technique is rarely used because of the high risk of PVR development in the postoperative period [103].

Tip: If a foreign body is not found during examination or surgery, it is most probably inferiorly located behind the iris, in the subretinal area, or at the angle, which may be discovered by the help of gonioscopy or scleral indentation (Fig. 8.17).

Subretinal

- Complete the vitrectomy prior to removal, and make sure that no vitreous attachment is left at the IOFB site.
- Create an extraction retinotomy.
- In an attached retina, retinotomy should be slightly larger than the size of the IOFB and placed on top of the IOFB site in order not to cause traction.
- In a detached retina, retinotomy may be placed away in an area where PVD exists. Viscoelastic use is recommended to create small retinal detachment between IOFB and retinotomy site temporarily, before moving the subretinal IOFB. Viscoelastics are superior to BSS in this setting, providing photoreceptor protection as well as giving the surgeon more control [80].
- Reattach the retina and laser the site of extraction retinotomy.
- Make sure that vitrectomy is complete and posterior hyaloid is removed in order to prevent postoperative PVR.
- Deep cautery can be applied to the choroid at the impact site (chorioretinectomy) to prevent PVR.

Tip: In some of the deeply localized IOFB cases, vitreous may be incarcerated into the impact site, making its removal impossible. It is safer to trim and leave vitreous focally here. Insisting on complete removal may result in retinal breaks, which should be avoided.

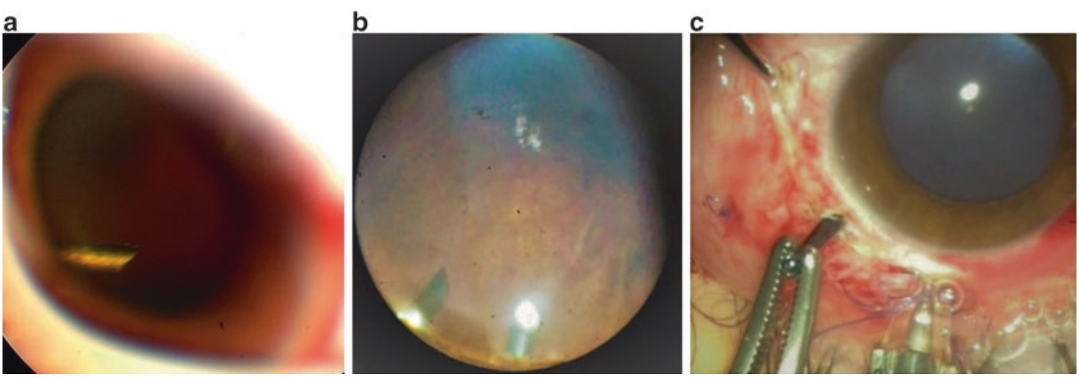

Fig. 8.17 Pencil tip stuck into the inferotemporal pars plana of a 10-year-old boy at school (**a**). Infusion cannula was placed next to the pencil tip (**b**). The suture of the primary repair at the entry site was cut, and the tip of the IOFB in the vitreous was grasped with a forceps to push out through the entry site backward. The outgoing part of pencil tip was grasped outside to remove from the eyewall (**c**)

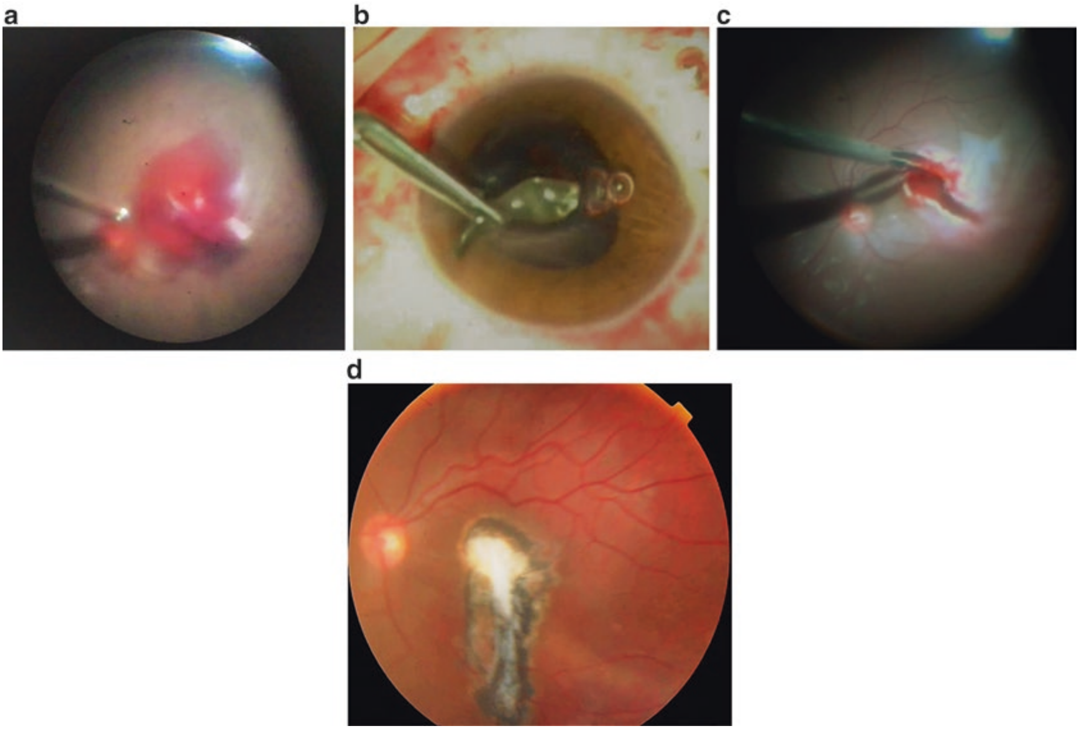

Fig. 8.18 Deep-impact IOFB was found embedded in the macula after removal of vitreous hemorrhage (**a**). Following complete vitrectomy, IOFB was transferred to AC by passive aspiration with flute cannula and extracted through limbal incision (**b**). Chorioretinectomy was performed even though the impact site was at the macula (**c**). Gas tamponade was used at the end of the surgery. Retina remained attached after silicone oil removal; neither PVR nor retinal folds were observed at 7 months postoperatively (**d**)

Choroidal/Scleral (Deep-Impact IOFBs)

Deep-impact IOFBs have two major risks to concern about:

- Intraoperative risk of iatrogenic retinal detachment and reopening of the scleral wound during the removal
- Postoperative risk of PVR development

Postoperative PVR risk is exceptionally high in deep impacts, despite complete or nearly complete vitreous removal. Prophylactic chorioretinectomy should be considered in any deep impact injury against proliferative vitreoretinopathy, as previously discussed [41–43] (Fig. 8.18).

8.4 Posttraumatic Endophthalmitis

8.4.1 Introduction

Posttraumatic infectious endophthalmitis is a devastating complication of an open-globe injury which has been reported to occur in 3.4% of open-globe injuries according to the US Eye Injury Registry [104].

Endophthalmitis in the setting of trauma differs profoundly from postoperative endophthalmitis in its microbiological profile and clinical course. Traumatic endophthalmitis carries a much poorer prognosis due to higher likelihood

of infection with more virulent organisms [105, 106], accompanying damage to ocular structures, and difficulty in diagnosis in the setting of an injured eye, hence the delay in the initiation of the treatment. Early recognition with prompt treatment is critical for recovery of the eye.

Tip: Clinicians should maintain a high suspicion of endophthalmitis after trauma since trauma-induced inflammation and tissue disruption might mask the infection. An increase in pain disproportionate to the trauma itself, inflammation, vitritis, and decrease in vision should suggest endophthalmitis. Close monitorization of the patient (even hourly) should be favored until the signs and symptoms improve or worsen to have a definite diagnosis.

8.4.2 Diagnosis

Diagnosis of endophthalmitis immediately after an open-globe injury can be difficult due to masquerading signs that usually accompany severe ocular trauma [105]. History-taking should focus on the circumstances of the injury and related risk factors that might suggest high probability of an infection, and symptoms should be sought well to identify early warnings.

8.4.3 Risk Factors

Many factors are found to be associated with increased risk for the development of endophthalmitis after open-globe injuries:

- *Retained IOFB* [54, 79, 107]. The composition of the FB and the timing of removal are also important as studies have shown higher risk of endophthalmitis if the FB is organic and removal of it exceeds 24 h [108].
- *Rural environment* [109]. An injury with a contaminated object is more likely in rural settings. Soil-contaminated injuries carry a high risk of infection with Bacillus species, which is highly virulent [109].
- *Delayed timing of primary repair*. Endophthalmitis is much less likely to develop in eyes with primary repair within 24 h of the injury (3.5%) than in eyes with primary repair more than 24 h after the injury (13.4%) [98, 107].
- *Lens disruption* [110, 111].
- *Primary IOL implantation* [52, 53].
- *Large wound size and location*. It has been shown that >8 mm wounds have increased risk for posttraumatic endophthalmitis [112]. Regarding location, Zhang and colleagues reported endophthalmitis in 5% of zone III injures in contrast to 14% of zone I injuries ($p < 0.001$) [107]. Zone III injuries might be protected against organisms by the overlying conjunctiva and Tenon's capsule.

8.4.4 Signs and Symptoms

- Pain is already present in the case of a trauma. However, pain disproportionate to the degree of injury should raise the suspicion of endophthalmitis; this may be the only finding of an early infection.
- Visual loss is another finding that can be related both to the trauma and endophthalmitis. Yet, further worsening of vision after primary closure, especially in the presence of increasing pain, suggests endophthalmitis.
- Clinical signs of infection include purulent discharge from the site of trauma, eyelid edema, chemosis, corneal edema, hypopyon and/or other signs of anterior chamber inflammation (pupillary membrane, posterior synechia), vitritis, retinitis, and periphlebitis. If infection progresses to panophthalmitis, signs of orbital cellulitis, such as limited range of ocular movement, proptosis, increased eyelid edema, and erythema, may be seen (Fig. 8.13c).
- Slowly progressive inflammation that is unresponsive to antibiotics and relatively mild pain may be indicative of fungal infections, especially if there is a history of soil

contamination or injury with organic matter [104, 113]. Characteristic “string of pearls” can be seen in vitreous.
- Rapid deterioration of infection in the presence of an IOFB and systemic signs such as fever and corneal ring ulcers suggest an infection with *Bacillus* species [52].
- Gas bubbles in the anterior chamber, greenish-brown hypopyon, and rapid progress are closely associated with *Clostridium* infection [52].

8.4.5 Microbiology

The organisms involved in posttraumatic endophthalmitis are typically more virulent compared to postoperative endophthalmitis, and multi-organism infections are also more frequent (15.6% [114]). Gram-positive organisms are the most common causative agents which consists of 75% of all posttraumatic culture-positive endophthalmitis [115]. The most common isolated organisms among Gram-positive species are *Staphylococcus epidermidis* and *Streptococcus* species [114]. Posttraumatic endophthalmitis caused by *Staphylococcus* species is more likely to have a favorable outcome compared to other organisms [111].

There is a high incidence of infection with *Bacillus* species (20%) in open-globe injuries, especially in the setting of an IOFB or soil contamination [116]. Bacillus infections are characterized by rapidly progressing (<24 h) severe endophthalmitis. Another organism that may cause fulminant endophthalmitis is *Clostridium* species, which is less commonly found [52].

Gram-negative organisms are less commonly involved in of posttraumatic endophthalmitis (0% to 33%) [114, 117]; however they are related to poor prognosis. Pseudomonas is the most commonly isolated organism in this group.

The incidence of fungal agents is reported to be between 0% and 15.4% [118]. Among them, the most common fungus is *Candida* but molds such as *Aspergillus* species, *Paecilomyces* species, and *Fusarium* species have also been reported [116].

8.4.6 Culturing

Samples of intraocular contents for cultures and stains should be obtained if endophthalmitis is suspected. However, it should be kept in mind that endophthalmitis is not microbiological but a clinical diagnosis. Positive culture results do not necessarily correlate with subsequent infection, and negative cultures do not mean that there is no infection as well [98, 119].

Samples should be plated on blood and chocolate agar as well as smears should be obtained for Gram, Giemsa, and fungal stains. Fungal infection can be detected by culturing on Sabouraud’s dextrose agar or potassium hydroxide (KOH) preparation [104]. DNA typing can also rapidly and effectively detect fungal pathogens [120].

Tip: Routine culturing at the time of primary closure of the wound is not cost-effective, as the finding of positive cultures does not predict outcome or change the management and false-positive results are high.

8.4.7 Prophylaxis

Currently, there is no consensus in the literature addressing the type and preferred route of administration of prophylactic antibiotics in eyes with open-globe injury. Immediate wound closure with systemic and topical antibiotic treatment seems to be the best approach to prevent post-traumatic endophthalmitis, even though this approach is not supported by strongly experimental evidence [121].

8.4.7.1 Systemic Prophylaxis

Systemic antibiotic of choice should have:

- Broad spectrum of coverage against the most common pathogens related to posttraumatic endophthalmitis such as Gram-positive organisms and *Bacillus* species

- Adequate intraocular penetration (injury to the globe may result in disruption of blood-retinal barrier that allows systemically administered antibiotics to reach eye more readily [122])

The ideal antibiotic regimen remains controversial:

- Intravenous use of third-generation cephalosporins (i.e., ceftazidime) and oral/intravenous fluoroquinolones demonstrates good intraocular penetration and adequate coverage against most of the common infective organisms in the setting of trauma, whereas most other antibiotics have limited penetration into the vitreous cavity [123–125].
- However, it should be kept in mind that while providing good Gram-negative coverage, intravenous ceftazidime provides poor coverage of *Bacillus* species [121, 125].
- Vancomycin, on the other hand, is efficient against Gram-positive organisms as well as *Bacillus* species and have been shown to reach adequate intraocular concentrations in inflamed eyes, when given intravenously [126].

We currently recommend the use of intravenous ceftazidime (1gr/8 h) concurrently with intravenous vancomycin (1 gr/12 h) for 1–3 days followed by a week of oral moxifloxacin at a dose of 400 mg/day as prophylaxis against infection.

An alternative approach is to use oral fluoroquinolones alone, which has been demonstrated to provide good intravitreal penetration and broad spectrum of coverage, as well as benefit of shortening the hospital stay [124, 127]. However, the use of oral medications may be limited in patients who cannot take oral medication prior to general anesthesia or if the patient has been nauseated.

> **Tip:** Routine antifungal prophylaxis is not recommended unless fungal endophthalmitis is suspected, regarding renal and retinal toxicity.

8.4.7.2 Intravitreal Prophylaxis

Routine intravitreal antibiotic administration at the time of primary wound repair followed by a week of oral antibiotics is advocated by some surgeons in an attempt to shorten the duration of hospitalization and allow outpatient management [128]. This setting is not widely accepted, but it may be preferred in selected cases which are at high risk for development of endophthalmitis (i.e., IOFB, contaminated injuries, delayed primary closure of the wound), provided that no choroidal or retinal detachments are present [98, 121].

8.4.8 Treatment

When endophthalmitis is clinically diagnosed, anterior and posterior chamber taps with intravitreal antibiotic injections should be performed urgently and early vitrectomy should be considered. Initial therapy of posttraumatic endophthalmitis is almost always empirical which is guided by the trauma setting, nature, and clinical signs. Once culture results are available, treatment can be modified according to the susceptibility of the organisms [52].

8.4.8.1 Medical Treatment

Antibiotics

Intravitreal, subconjunctival, topical, and systemic antibiotics are recommended (details of current empirical treatment outlined in Table 8.6). Intravitreal antibiotics are the first line of therapy as they enable the highest amount of drug delivery into the vitreous compared to other routes of administration [129]. Currently, recommended empirical intravitreal treatment is the combination of vancomycin with ceftazidime [52]. Vancomycin covers all Gram-positive organisms while having little resistance [130] and ceftazidime provides adequate Gram-negative coverage including *Pseudomonas*. However, because *Bacillus* species usually are resistant to cephalosporins [131], amikacin (0.4 mg/0.1 ml) may be considered in addition to vancomycin in cases of *Bacillus* endophthalmitis [52].

Table 8.6 Treatment of bacterial traumatic endophthalmitis[a]

Route of administration	Drug	Dose
Intravitreal injection	Ceftazidime	2.25 mg/0.1 ml
	Vancomycin	1 mg/0.1 ml
	Dexamethasone	0.4 mg/0.1 ml
Vitrectomy infusion fluid[b]	Ceftazidime	0.45 mg/ml
	Vancomycin	0.2 mg/ml
	Dexamethasone	0.04–0.08 mg/ml
Subconjunctival	Ceftazidime	100 mg/0.5 ml
	Vancomycin	25 mg/0.5 ml
	Dexamethasone	15 mg/1 ml
Topical	Fortified topical antibiotics (ceftazidime, vancomycin)	50 mg/ml, every hour
	Moxifloxacin	0.5%, every hour
	Prednisolone acetate	1%, every hour
	Cycloplegics	Several times daily
Oral	Moxifloxacin	400 mg, once daily
Intravenous	Ceftazidime	1 g, every 8 h
	Vancomycin	1 g, every 12 h

[a]Treatment must be modified once the results of culturing becomes available
[b]An alternative to using intravitreal antibiotics at the end of the case is adding antibiotics into the infusion fluid

Tip: Vancomycin and ceftazidime should be given in two separate syringes in order not to cause precipitation of antibiotics.

Fortified topical antibiotics should be applied in conjunction with intravitreal antibiotics. Topical fluoroquinolones may substitute fortified antibiotics according to clinician's preference [132]. Topical ciprofloxacin (third generation) or moxifloxacin (fourth generation) is used on hourly basis. Our approach is to use topical fortified vancomycin and ceftazidime for the first few days until the clinical picture of endophthalmitis begins to subside and continue with topical moxifloxacin thereafter. We do not routinely use subconjunctival antibiotics; however, they can be an alternative in patients where frequent drops cannot be administered [52].

Steroids

There is no consensus in the literature regarding any aspect of steroid use, the timing, dosing, or the route of administration. Treatment of infection with antibiotics leads to release of products of the dying bacteria (i.e., endotoxins) which can cause additional inflammation and ocular damage [133]. Host inflammatory response further exacerbates the condition as well. Hence, controlling the inflammation may result in more favorable outcomes.

On the other hand, a potential disadvantage is that steroids may suppress the immune system, impeding infection control, especially when the organism is not susceptible to the empirical treatment as in fungal endophthalmitis. Some clinicians prefer deferring steroid treatment until 12 h after administration of antibiotics to allow them to take action [52].

Overall, steroids may be beneficial to reduce the inflammation and fasten recovery. In practice, intravitreal steroids are more commonly used than systemic steroids to eliminate side effects [133]. We recommend routine use of intravitreal dexamethasone in traumatic endophthalmitis unless there is suspicion of fungal infection. Once the intravitreal antibiotics are administered, topical steroid drops are started on hourly basis, until the inflammation starts to subside and then tapered. If fungal endophthalmitis is suspected, steroid treatment should be withheld [52].

Our approach is to use intravitreal 0.4 mg/0.1 ml of dexamethasone injection together with intravitreal antibiotic injections routinely.

Antifungals

Unlike therapy for bacterial traumatic endophthalmitis, which is delivered at the time that specimens are collected, therapy for fungal endophthalmitis is never instituted unless there is very high clinical suspicion (e.g., organic matter, indolent symptoms) or microbial evidence, in order to avoid the potential posterior segment toxicity.

Intravitreal amphotericin B (5 μg/0.1 ml) combined with systemic amphotericin B (1 mg/kg, in divided doses daily) and topical amphotericin B drops (1.5 mg/ml, hourly) is the most common treatment regimen in posttraumatic fungal endophthalmitis [134]. Alternatively, the use of intravitreal voriconazole (50 μg/0.1 ml), combined with oral voriconazole (200 mg, twice daily), provides adequate coverage against frequent organisms (i.e., *Candida*, *Aspergillus* spp.) [135], with less retinal and renal toxicity [136].

8.4.8.2 Surgical Treatment

In addition to appropriate antibiotic treatment, many ophthalmologists, like us, advocate early vitrectomy in the setting of traumatic endophthalmitis [24, 104, 134] in an attempt to:

- Remove the infectious and inflammatory load
- Allow better distribution of antibiotics
- Remove the vitreous scaffolding that may cause tractional membranes
- Repair concurrent intraocular damage requiring vitrectomy

Vitrectomy can be technically difficult due to poor visualization (e.g., corneal edema, anterior chamber inflammation, disrupted lens, hazy media). In these cases, scraping the corneal epithelium, irrigation of anterior chamber, removal of the fibrinous membranes and inflammatory debris with a blunt cannula or vitrectomy probe (along with the use of AC maintainer), and removal of disrupted lens may help (Fig. 8.19). If the cornea still does not allow visualization, temporary keratoprosthesis may be necessary followed by penetrating keratoplasty.

> **Tip:** In cases of fungal endophthalmitis, antifungal treatment is generally not enough to clear the infection once there is significant vitreous invasion [24, 96]. Hence, vitrectomy should be the primary treatment of choice in these cases, with the addition of medical therapy.

> **Tip:** It is important to obtain samples in the beginning of the vitrectomy, even before activating the infusion line. At this stage using air instead of balanced salt solution might protect the intraocular pressure, without diluting the intraocular contents that are being aspirated.

8.4.9 Controversies Regarding Vitrectomy

8.4.9.1 Timing of Surgery

There is no doubt that in a case of IOFB or retinal detachment, prompt vitrectomy should be the treatment of choice [68]. Nevertheless, we recommend early vitrectomy, if not immediate, regardless of the presence of IOFB, which will enable the treatment of the infection and ocular injuries at the same time.

> **Tip:** Following a proper injection and tap procedure, if there is no clinical improvement with close monitoring of the eye (even hourly), immediate vitrectomy should be considered.

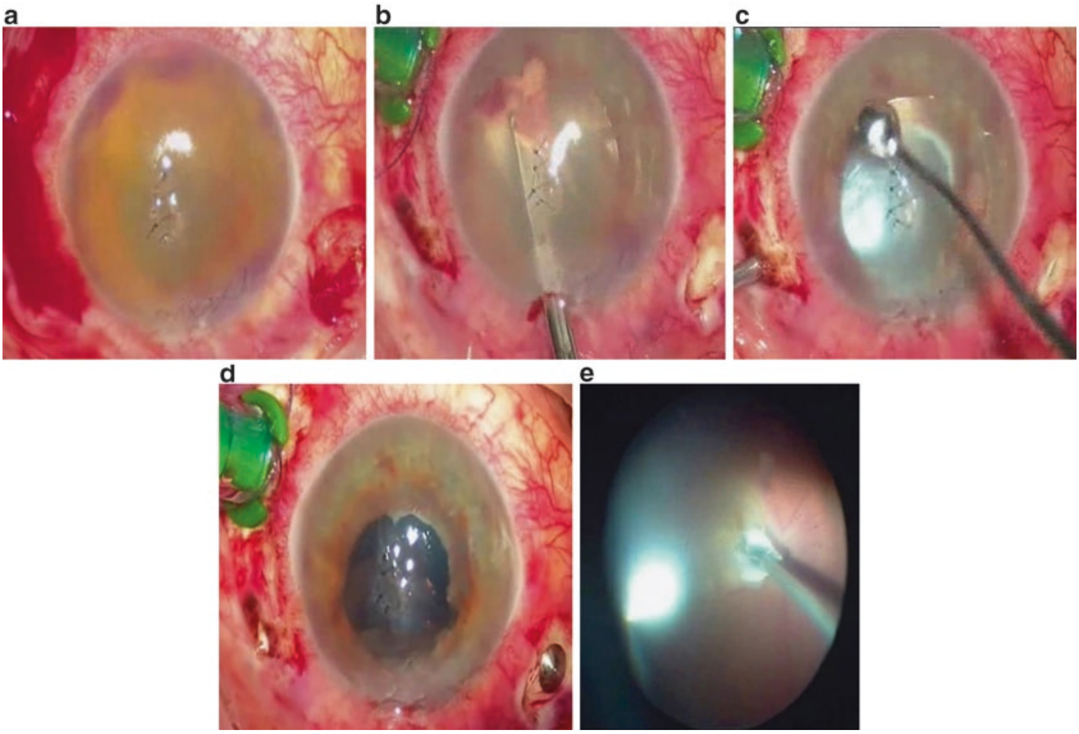

Fig. 8.19 A 12-year-old boy referred to us with posttraumatic endophthalmitis and the presence of an IOFB. Visual acuity was light perception. Cornea was so cloudy that it did not allow visualization of posterior segment. Presence of inflammatory membranes covering the pupillary area further blocked the view (**a**). Removal of fibrinous inflammatory membranes from the anterior chamber and the back of the lens (**b**) and scraping the corneal epithelium (**c**) cleared the view (**d**) which made vitrectomy possible without the need for penetrating keratoplasty. After removal of central vitreous opacities, the retina could be visualized enough to take the IOFB out and to perform a vitreoretinal surgery (**e**). The eye was left with silicone oil and 1/3 dose of intravitreal vancomycin and ceftazidime at the end of the procedure. Silicone oil was removed 3 months later. Retina remained attached at long-term follow-up; however, best-corrected visual acuity remained 20/400 because of the macular scar (Reproduced with the permission from Yan H. Mechanical Ocular Trauma. Springer; Springer Science+Business Media Singapore; 2017)

8.4.9.2 Extend of Surgery

- Extend of vitrectomy should be adjusted according to each case, as general approach; vitreous should be debulked as complete as it can be safely.

A limited core vitrectomy should be the choice if retina is severely inflamed with intraretinal hemorrhages and cotton wool spots [118]. Inflamed retina may be exceptionally fragile and prone to tears and detachment; hence, the surgeon should not be too aggressive while removing the peripheral vitreous.

Posterior hyaloid should be separated if possible. If the retina is necrotic and fragile and vitreous is very adherent, this procedure is better be left. Sequential vitrectomies may be performed in severe cases, in order to be on the safe side. However, it is important to make individual decisions for each case. For instance, in a case with significant debris under internal limiting membrane (ILM), ILM peeling may be considered with caution if the retinitis is of low grade (Fig. 8.20).

8.4.9.3 Silicone Oil Use as Tamponade

Using silicone oil at the completion of vitrectomy has been shown to be beneficial in the presence of rhegmatogenous retinal detachment or high risk of retinal tear formation and due to its antimicrobial properties [137, 138]. We suggest using silicone oil tamponade in all cases of endo-

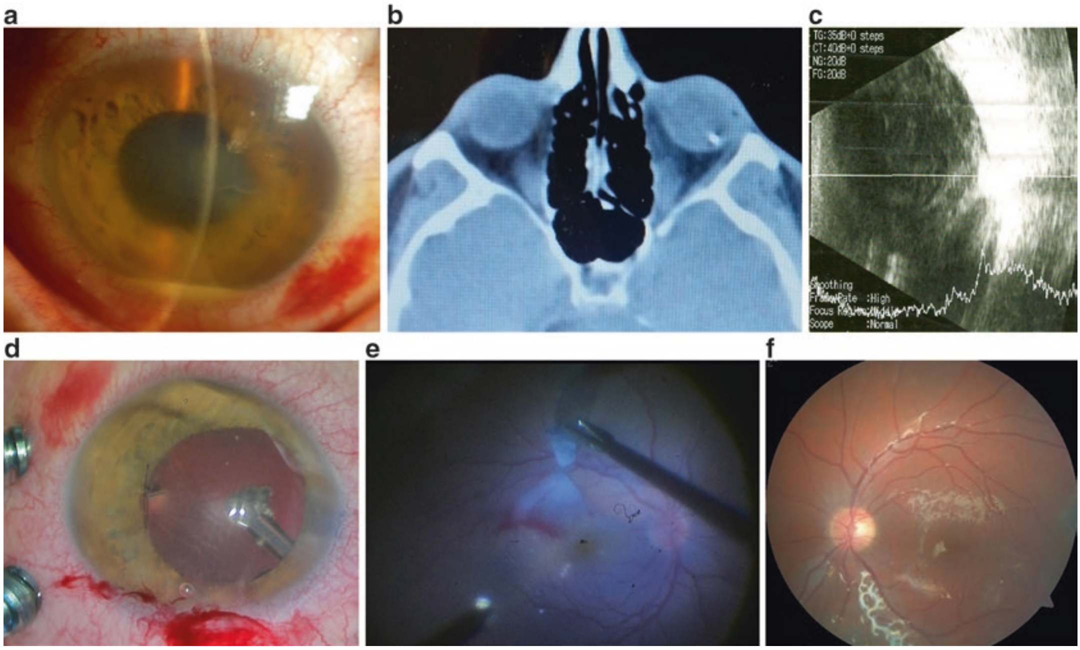

Fig. 8.20 A 38-year-old male presented with clinical signs of infection (conjunctival hyperemia, severe anterior chamber inflammation, hypopyon, and vitritis) 3 days after a penetrating trauma (**a**). Visual acuity was hand motions and corneal wound was observed to be self-sealing with negative Seidel test. Intravitreal tap and injection (vancomycin, ceftazidime, and dexamethasone) were performed immediately. CT showed a metallic IOFB (**b**). B-scan ultrasound showed severe vitreous inflammation with attached retina and a hyperechoic foreign body with shadowing (**c**). Pars plana vitrectomy was performed the next day with lensectomy and IOFB removal through AC (**d**). Mild retinitis and sub-ILM inflammatory debris were observed. Removal of ILM with the help of ILM-blue was needed to clear the inflammatory debris (**e**). Silicone oil tamponade was used at the end of surgery. Clinical picture of endophthalmitis subsided rapidly, (**f**) and best corrected visual acuity improved to 20/32 at 1 month postoperatively(Reproduced with the permission from Yan H. Mechanical Ocular Trauma. Springer; Springer Science+Business Media Singapore; 2017)

phthalmitis with significant retinitis, even in the absence of retinal breaks, because of its antimicrobial properties. For those without significant retinitis, air tamponade may be used instead, which we believe also has some anti-inflammatory effect [118, 139].

> **Tip:** When silicone oil is used as tamponade, intravitreal antibiotic and dexamethasone doses should be reduced by 1/3–1/10 of the normal dose in order to reduce retinal toxicity.

8.4.10 Recommended Approach

Empirical treatment should be started right away in the suspicion of a traumatic endophthalmitis. Following IV tap, our first-line treatment is intravitreal vancomycin, ceftazidime, and dexamethasone injections unless there is suspicion of fungal endophthalmitis. Topical fortified antibiotics and steroid drops on hourly basis should be introduced along with cycloplegics. For systemic treatment, we generally use intravenous ceftazidime combined with intravenous vancomycin. If organic matter is the cause of the trauma and the

presenting symptoms are indolent, fungal endophthalmitis should be suspected and treated with intravitreal amphotericin B and/or intravenous voriconazole.

We prefer immediate vitrectomy (with silicone oil in cases with severe retinitis or vasculitis) in posttraumatic endophthalmitis if possible, regarding multiple and more virulent organisms in the etiology and associated intraocular injuries. If this is not possible immediately, we inject intravitreal antibiotics and steroid until becoming ready for the surgery. Intravitreal AB injections at a reduced dose at the end of the surgery or, alternatively, addition of antibiotics to the infusion fluid can be used.

Empirical treatment should be modified once the culture results are available. If no improvement noted within 48–72 h despite appropriate antibiotic treatment, we recommend repeating vitrectomy for further debridement of the infectious material in the vitreous, especially if a limited vitrectomy was performed initially.

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9 Chemical Injuries of the Cornea

Weiyun Shi and Suxia Li

Abstract

Chemical injuries of the ocular surface are very common in China. Acids and alkalis are frequently encountered offending chemical agents. It is very difficult to treat chemical burns of the ocular surface for lack of ideal approaches. This chapter introduces the clinical features of chemical injuries and first aid and subsequent treatment of chemical injuries.

Keywords

Chemical injuries · Acids burns · Alkalis burns · Amniotic membrane transplantation; keratoplasty

9.1 Introduction

Chemical injuries of the ocular surface are very common in China. Despite the emergency treatment immediately after the burns, many patients lose their vision because of complete destruction of the eye. Acids and alkalis are frequently encountered offending chemical agents. It is very difficult to treat alkali burns of the ocular surface for lack of ideal approaches. Patients with severe injuries often suffer blindness at late stages due to corneal opacity, perforated ulceration, corneal neovascularization, pseudopterygium ingrowth, and symblepharon.

9.1.1 Types of Chemical Injuries

- Acidic substances: sulfuric acid, hydrochloric acid, nitric acid, phosphoric acid, etc.
- Alkaline substances: (1) alkali metals (sodium, potassium, potassium hydroxide, etc.), (2) alkaline earth metals (calcium, calcium hydroxide, calcium chloride, etc.), and (3) ammonia (ammonium hydroxide, ammonium chloride, etc.)
- Nonmetallic mordants: phosphorus and its compounds

9.1.2 Factors Related to the Severity of Ocular Chemical Injuries

The severity and prognosis of ocular chemical injuries are associated with many factors, including the property of the chemical, the area of the injury, and the emergency treatment.

- In general, the longer the chemical stays in the eye, the greater the eye injury is. Meanwhile, the larger the trauma is, the severer the damage to ocular tissues is.
- The penetration of acidic and alkaline substances to ocular tissues is various due to their

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different chemical properties, so the damage and prognosis are not the same. Alkali burns are usually worse than acid burns.
- The concentration of the chemical and the resistance of different parts of the eye to the acidic or alkaline substances also have an impact on the injury severity.

9.1.3 Pathological Damage in the Late Stage of Chemical Injury of the Ocular Surface

- Damage to the conjunctiva. Because corneal limbal stem cells and goblet cells are seriously destroyed, the epithelium of the conjunctiva, a translucent smooth mucosal membrane, is replaced with a number of abnormally proliferated fibroblasts with no conjunctival function. Due to conjunctival goblet cell loss, the tear film is damaged. When the conjunctival necrosis area is over 1/2 of the limbal stem cells, regeneration of the corneal epithelium will not only become slow but also lead to corneal conjunctivalization with characteristics of epithelial opacification, accompanied by many goblet cells and corneal pannus. Even if the tear secretion is normal, abnormal corneal goblet cells can cause corneal instability and conjunctival abnormality.
- Damage to the cornea. The corneal epithelium may suffer the same damage as the conjunctiva. Necrosis and sloughing occur after the epithelium contacts with alkaline substances, and the epithelial defects can directly reflect the location and area of chemical burns. Corneal stromal collagen lamellae are destroyed after the trauma, which is aggravated with abnormal immune response and eventually replaced with fibrotic scarring. Loss of endothelial cells reduces the physiological function, resulting in persistent corneal edema, neovascularization, and even corneal vascularization and vascular membrane coverage [1, 2].
- Damage to the tear film. Due to the damage to conjunctival goblet cells, accessory lacrimal glands (glands of Krause and Wolfring), and corneal epithelium, it is difficult to form the tear film. The openings of the accessory lacrimal glands and all or part of the lacrimal glands are under the conjunctival fornix. Adhesion and scar formation reduce tear secretion significantly, causing substantial dryness in the eye, which is manifested as Schirmer tear secretion less than normal, failure to form the tear film, tear breakup time anomaly (<10 s), or positive rose bengal test result. Patients with severe xerophthalmia usually show epithelial keratinization and conjunctival dryness with folds.
- Corneal neovascularization. Mild and moderate alkaline burns can induce neovascularization in all or part of the cornea. Severe cases may also have the cornea covered by fibrous vascular membrane. There are two kinds of theories about the mechanism of neovascularization. One is leukocyte mediation. Leukocyte infiltration is thought to occur before the generation of new blood vessels. Another is angiogenesis growth factors, which stimulate growth of new blood vessels, including fibroblast growth factor, platelet-derived growth factor, and transforming growth factor. Further investigations are under way [3, 4].
- Symblepharon. Part of adhesions occur in patients with mild burns, while in severe cases both upper and lower eyelids stick with the eye globe, resulting in complete fixation of the eye and closure of the palpebral fissure [5].
- Other intraocular complications. Secondary glaucoma is a very serious complication. Destruction of the chamber angle tissue may increase intraocular pressure [6, 7]. However, most doctors only pay attention to the abnormal changes of the external eye and neglect measurement of intraocular pressure. When it is feasible to reconstruct the anterior segment, patients are likely to lose the opportunity of sight recovery because of optic atrophy. Another complication is complicated cataract. Extracapsular cataract extraction combined with intraocular lens (IOL) implantation can be performed simultaneously with penetrating keratoplasty or later. With corneal edema, opacity, and neovascularization, most eyes could not be adequately detected before sur-

gery. Whether to implant an IOL has to be determined intraoperatively. As long as the iris is basically healthy, IOL implantation is recommended during keratoplasty.

9.2 Clinical Features of Chemical Injuries

The most common chemical injuries are acid and alkali burns, and the latter seems to be more refractory. Understanding the pathological process of chemical burns is beneficial to clinical treatment and prognosis.

9.2.1 Pathological Process

Alkali as fat-soluble substance can cause damage in three aspects when in contact with the eye. First, rapid solidification of tissue proteins and cell necrosis may occur. Its function of dehydration makes the extracellular and intracellular fluids imbalanced, accelerating cell necrosis. Second, saponification of alkali substance and lipoids in the tissue can break the structure of cell membrane. The softening or liquefied environment stimulates the alkali to diffuse to and injure the surrounding and intraocular tissue. Third, blood clots form in the normal ocular blood vessels, causing ischemia and nutrient deficiencies of the cornea, accelerating tissue damage and hindering repair. Acid is water soluble and not easy to penetrate the corneal epithelium which is rich in lipoids, so the damage is generally confined to the epithelial tissue it contacts. However, strong acid with a low pH level often destroys the corneal epithelium, penetrates into the corneal stroma, and causes irreversible stromal denaturation and protein precipitation, which can prevent the acid from entering the inner eye further. Due to the coagulation, tissue edema and decomposition are comparatively mild, and the injured tissue boundary is obvious. Acid burns are often less severe and lead to fewer intraocular complications compared to alkali burns.

9.2.2 Clinical Manifestations, Staging, and Grading

Taking alkali burn as an example, when the pH value is more than 11, the matrix mucopolysaccharide is rapidly destroyed, and the collagen fibers are swollen. Within 3–5 min after NH_3 burn, the pH level of aqueous humor in the anterior chamber can increase. The anterior chamber irrigation should be adopted as soon as possible.

There has been no uniform standard about the staging of alkali injury of the anterior segment at home and abroad. We propose to divide alkali burns into three stages and four grades, with the time, degree, and treatment principle of injuries involved.

- The acute stage (early stage). From the pathological point of view, within 1 week after alkali burn, there are acute tissue necrosis and aseptic inflammatory exudation. According to the injury area and the degree of corneoscleral ischemia, the stage can be classified into four grades (Figs. 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, 9.10, 9.11, 9.12, 9.13, 9.14, 9.15, 9.16, 9.17, 9.18, 9.19, 9.20, 9.21, 9.22, 9.23, 9.24, 9.25 and 9.26).

Grade I: Good prognosis; corneal epithelial defect; no conjunctival ischemia.
Grade II: Good prognosis; decreased corneal transparency but visible iris texture; ischemic conjunctival area < 1/3 corneal limbus.
Grade III: Poor prognosis; complete corneal epithelial defect; opaque corneal stroma and invisible iris texture; ischemic conjunctival area accounting for 1/3 to 1/2 corneal limbus.
Grade IV: Poor prognosis; corneal opacity and invisible iris and pupil; ischemic conjunctival area > 1/2 corneal limbus.

Clinical Manifestations Within 1 week after alkali burn, alkaline saponification destroys the cell membranes of all corneal layers, ciliary body, and trabecular meshwork, with limbal and conjunctival ischemia. Corneal edema, haze or pale conjunctiva, fibrinoid exudation in the anterior chamber, and even cataract are observed. After severe burns, there is intraocular pressure elevation. The possible

reasons are aqueous prostaglandin increase, corneal and scleral collagen shrinkage, and obstruction or atresia of the aqueous humor outflow. Therefore, in the acute stage, attention should be given to measurement and management of intraocular pressure (Figs. 9.1, 9.2, 9.3, 9.4, 9.5, 9.6, 9.7, 9.8, 9.9, 9.10, 9.11 and 9.12) [8].

- The stage of coexisted damage and repair (intermediate stage). Pathologically, inflammatory cell infiltration, hyperplasia, and repair coexist, accompanied by further damage to visual function, between week 2 and week 6. The epithelial cells are replaced with the fibrous tissue. There are a lot of new blood vessels and vascular membranes in the cornea. Damage to the tear film brings drying changes. Autoimmune reaction and collagenase increase lead to corneal autolysis and perforation. Secondary bacterial infections and other complications may also occur. The procedure and duration of the above alternations depend on the degree of alkali injury and acute stage management. The major treatment in this stage remains to be inflammation control and appropriate surgical intervention for symptoms and complications, such as inhibition of collagenase activity, use of corticosteroids, prevention of bacterial infection, excessive symblepharon, and secondary glaucoma.

Clinical Manifestations This stage is featured with coexistence of tissue necrosis and repair. In

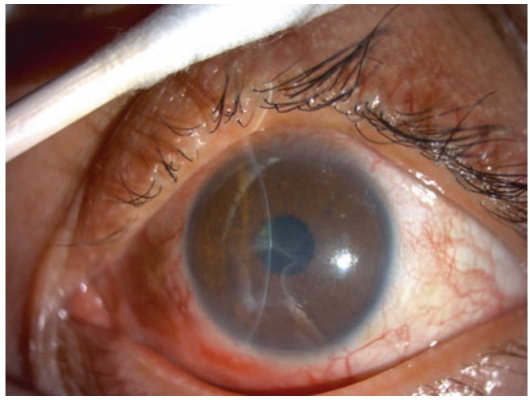

Fig. 9.2 Conjunctival congestion accompanied by central corneal epithelial defects in the acute stage (early stage) of chemical burn graded I

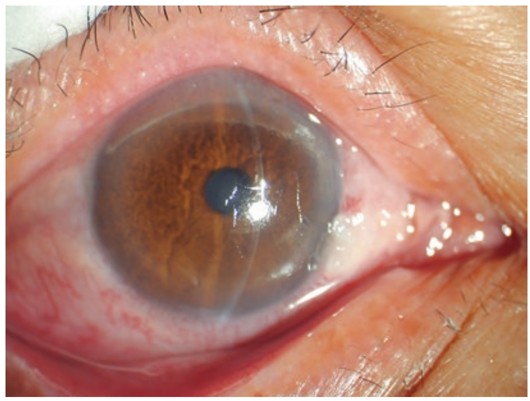

Fig. 9.3 Conjunctival congestion but no corneal epithelial defect in the acute stage (early stage) of chemical burn grade I

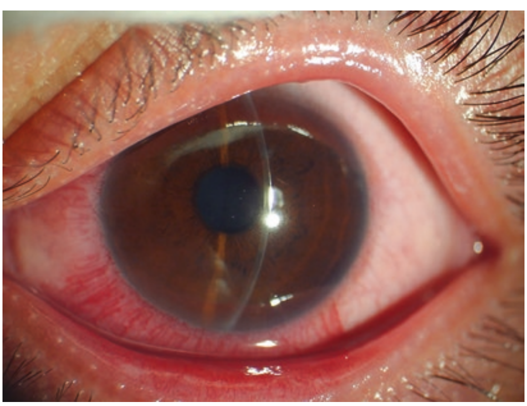

Fig. 9.1 Conjunctival congestion but no corneal epithelial defect in the acute stage (early stage) of chemical burn grade I

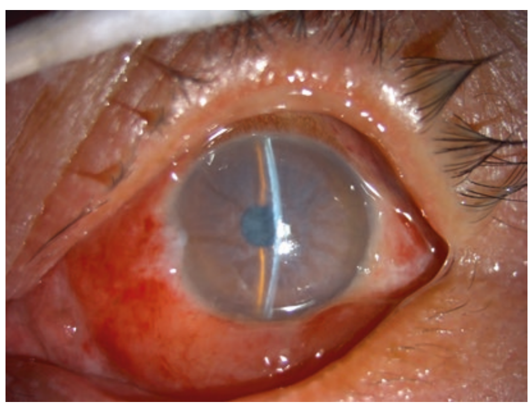

Fig. 9.4 Conjunctival congestion, total corneal edema, epithelial defects, and Descemet's membrane folds in the acute stage (early stage) of chemical burn graded II

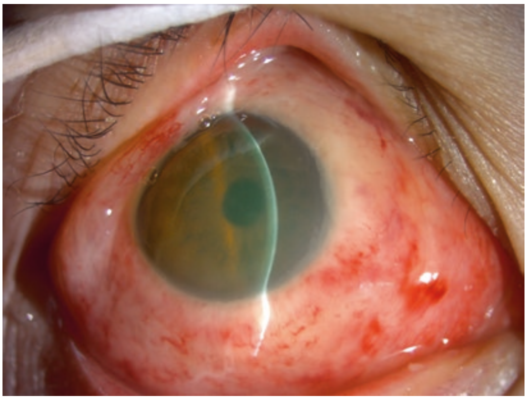

Fig. 9.5 Mild ischemia and slice-shaped bleeding of the conjunctiva, accompanied by total corneal edema and epithelial defects in the acute stage (early stage) of chemical burn graded II

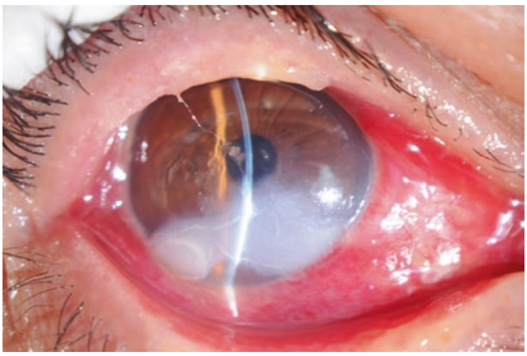

Fig. 9.6 Conjunctival congestion and localized corneal opacity and edema with epithelial defects in the acute stage (early stage) of chemical burn graded II

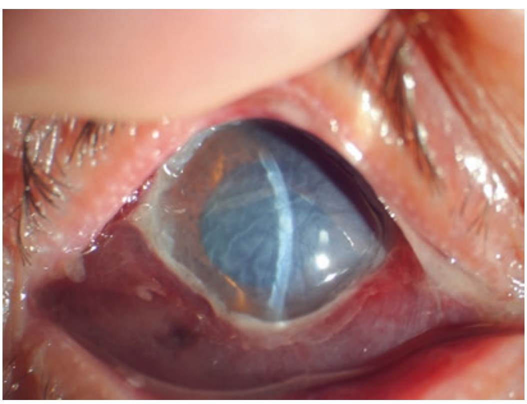

Fig. 9.7 Total corneal epithelial defects, edema, opacity, and Descemet's membrane folds after subconjunctival injection of serum in the acute stage (early stage) of chemical burn graded III

Fig. 9.8 Conjunctival congestion, total corneal edema and opacity, Descemet's membrane folds, and central epithelial defects in the acute stage (early stage) of chemical burn graded III

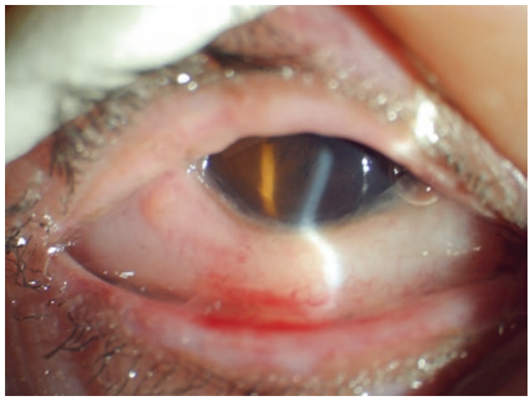

Fig. 9.9 Severe edema and ischemia of the bulbar conjunctiva and the clear cornea with total epithelial defects in the acute stage (early stage) of chemical burn graded III

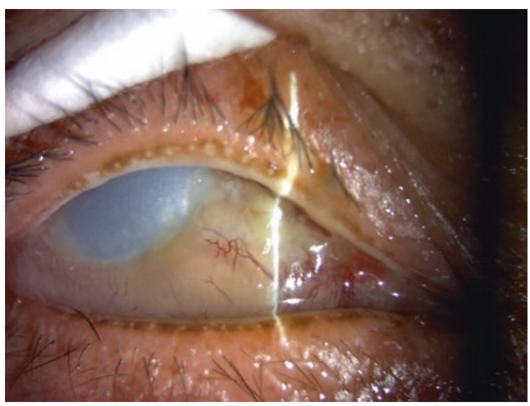

Fig. 9.10 Extensive ischemia and vascular occlusion in the pale palpebral and bulbar conjunctiva, accompanied by the gray-white and opaque cornea with total epithelial defects in the acute stage (early stage) of chemical burn graded IV

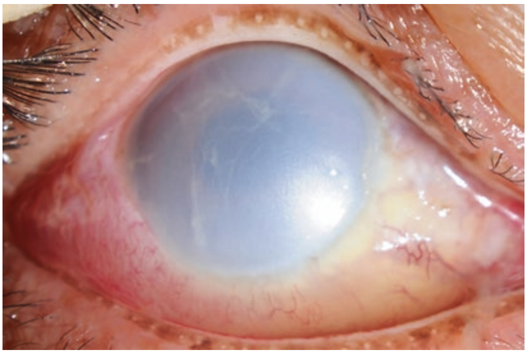

Fig. 9.11 The pale and ischemic palpebral and inferior nasal bulbar conjunctiva with vascular occlusion; the gray-white cornea with total epithelial defects, opacity, and edema; and the almost invisible pupil in the acute stage (early stage) of chemical burn graded IV

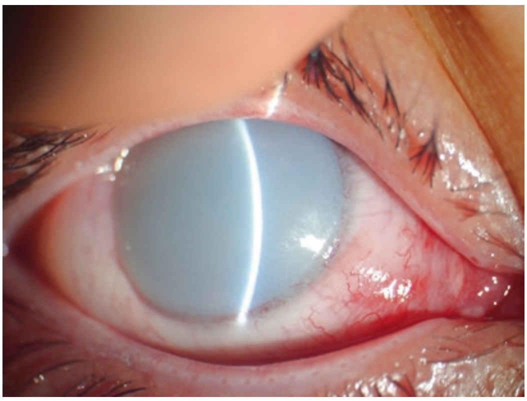

Fig. 9.12 The extensively pale and ischemic bulbar conjunctiva with thinning blood vessels; the gray-white cornea with total epithelial defects, opacity, and edema; and the invisible intraocular tissue in the acute stage (early stage) of chemical burn graded IV

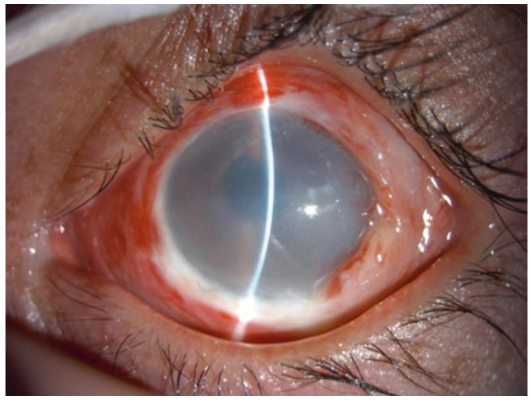

Fig. 9.13 Ischemia at 1/3 of the junction of corneal limbus and bulbar conjunctiva and congestion in the other conjunctival area, accompanied by corneal opacity and epithelial non-healing in the stage of coexisted damage and repair (intermediate stage) of chemical burn

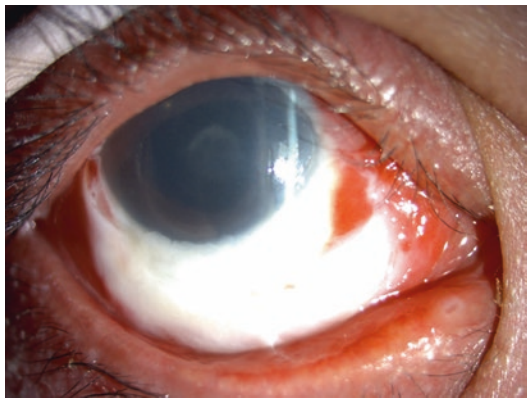

Fig. 9.14 A large area of ischemia in the inferior corneal limbus, bulbar conjunctiva, and sclera, conjunctival necrosis, corneal opacity, epithelial non-healing, and pupil dilation in the stage of coexisted damage and repair (intermediate stage) of chemical burn

grade I and II burns, degenerated keratoconjunctival epithelium begins to repair, new blood vessels proliferate, and the stroma keeps transparent. Iritis may occur because usually the iris is also burned. Involvement of ciliary body often causes hypopyon and lesions. In grade III and IV burns, corneal epithelial cells cannot regenerate, corneal stroma suffers persistent edema and opacity, and fiber cell membrane substitutes for the necrotic corneal endothelium. Damage to limbal stem cells hinders the corneal epithelial repair in severe cases, leading to abnormal release of collagenases and metalloproteins and thus stromal ulceration. Moreover, activation of fibrous proteins can induce corneal lamellar fibrous dissolution and even corneal autolysis and perforation (Figs. 9.13, 9.14, 9.15, 9.16, 9.17, 9.18, 9.19, 9.20, 9.21, 9.22 and 9.23).

- The stable stage (late stage). Pathologically, in this stage the status of tissue injury and repair

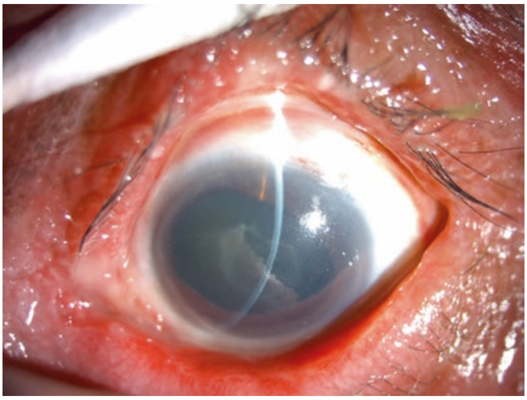

Fig. 9.15 Ischemia in the circumcorneal zone, corneal turbidity, epithelial non-healing, pupil dilation, and lens opacity in the stage of coexisted damage and repair (intermediate stage) of chemical burn

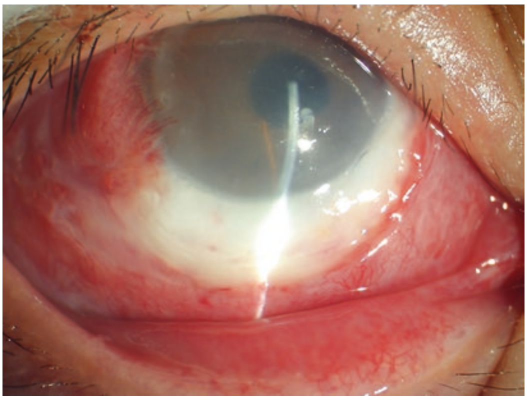

Fig. 9.16 Ischemia in the inferior corneal limbus and bulbar conjunctiva, growth of new blood vessels in the other limbal area toward the cornea, corneal opacity, and epithelial non-healing in the stage of coexisted damage and repair (intermediate stage) of chemical burn

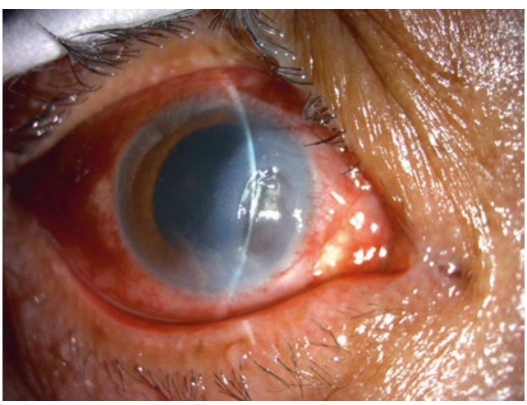

Fig. 9.17 Congestion of the bulbar conjunctiva, opacity in half of the nasal cornea, and 5 mm to 6 mm central ulceration in the stage of coexisted damage and repair (intermediate stage) of chemical burn (Adapted from the photo library of Shandong Eye Hospital, Shandong, China)

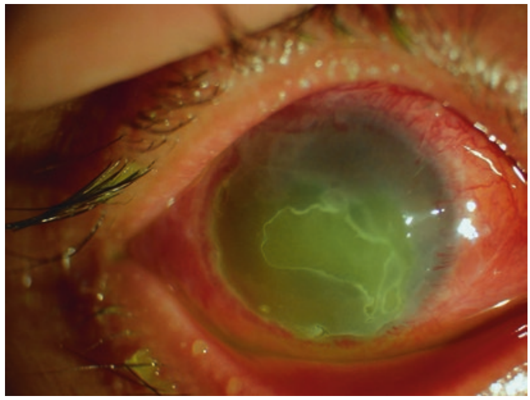

Fig. 9.18 Congestion of the bulbar conjunctiva, new blood vessel growth in the periphery, and irregular ulceration and opacity in the central cornea in the stage of coexisted damage and repair (intermediate stage) of chemical burn (Adapted from the photo library of Shandong Eye Hospital, Shandong, China)

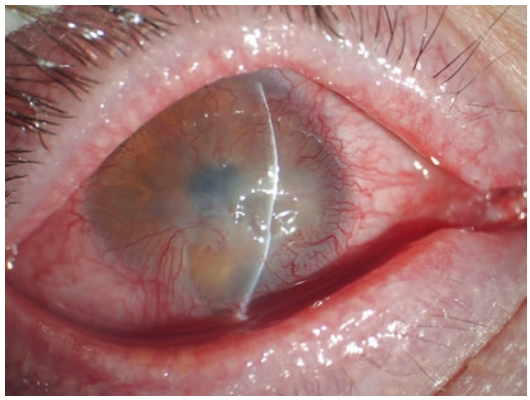

Fig. 9.19 Circumcorneal new blood vessel growth into the pupil area with temporal corneal ulceration in the stage of coexisted damage and repair (intermediate stage) of chemical burn (Adapted from the photo library of Shandong Eye Hospital, Shandong, China)

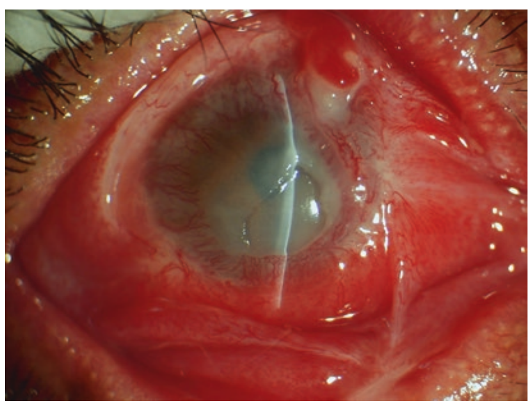

Fig. 9.20 Congestion and scarring of the bulbar conjunctiva with a polyp in the superior, circumcorneal new blood vessel growth and inferior nasal corneal ulceration in the stage of coexisted damage and repair (intermediate stage) of chemical burn (Adapted from the photo library of Shandong Eye Hospital, Shandong, China)

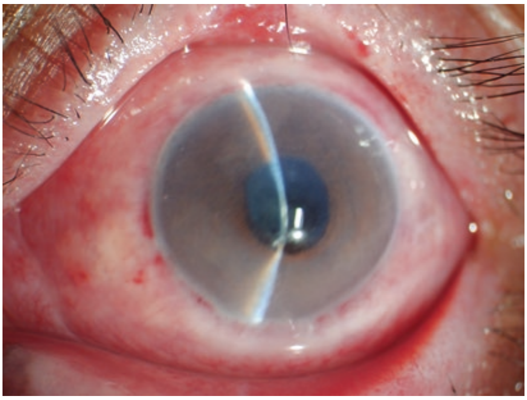

Fig. 9.21 Bulbar conjunctival ischemia and scarring, total corneal dissolution, obvious central thinning, and perforation in the stage of coexisted damage and repair (intermediate stage) of chemical burn (Adapted from the photo library of Shandong Eye Hospital, Shandong, China)

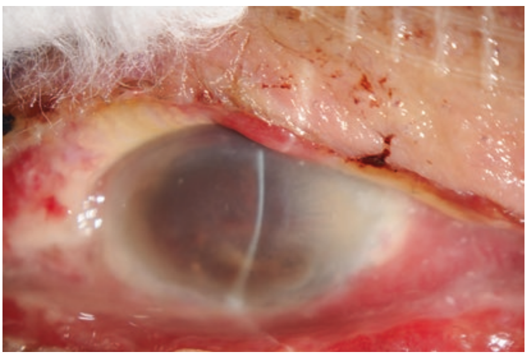

Fig. 9.22 Bulbar conjunctival ischemia and scarring, total corneal dissolution, perforation, and uveal incarceration in the stage of coexisted damage and repair (intermediate stage) of chemical burn (Adapted from the photo library of Shandong Eye Hospital, Shandong, China)

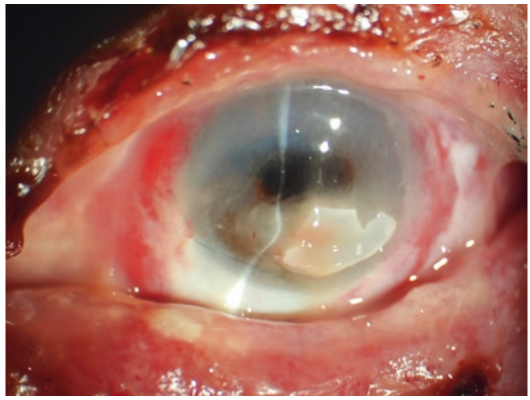

Fig. 9.23 Bulbar conjunctival ischemia and scarring, total corneal dissolution, central perforation, and intraocular tissue prolapse in the stage of coexisted damage and repair (intermediate stage) of chemical burn (Adapted from the photo library of Shandong Eye Hospital, Shandong, China)

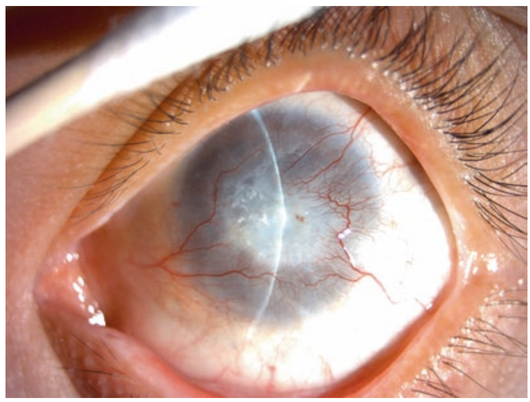

Fig. 9.24 No congestion in the bulbar conjunctiva, circumcorneal new blood vessel ingrowth, and central corneal leukoma, with no visibility of the pupil in the stable stage (late stage) of chemical burn (Adapted from the photo library of Shandong Eye Hospital, Shandong, China)

is relatively stable with sequelae on week 6 to week 12 following alkaline injury. The stability depends on both the severity of trauma and appropriateness of management in the acute and intermediate stages. Surgical intervention is the main approach.

Clinical Grading and Manifestations At 3 months after chemical injury, patients in grade I and II often heal completely without complications. For patients in grade III and IV, besides persistent tear film abnormality, secondary glaucoma, and cataract, the cornea presents with no healing of the epithelium, edema, opacity, expanding ulceration, and stromal neovascularization. In a later period, symblepharon and corneal neovascularization may occur, as well as corneal pannus covering the entire burn area (Figs. 9.24, 9.25 and 9.26).

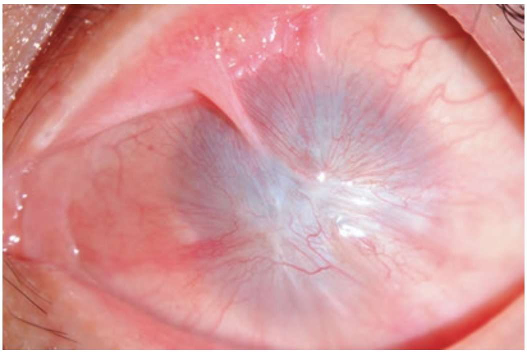

Fig. 9.25 Superior symblepharon and pseudopterygium covering the cornea, with invisibility of the intraocular tissue in the stable stage (late stage) of chemical burn (Adapted from the photo library of Shandong Eye Hospital, Shandong, China)

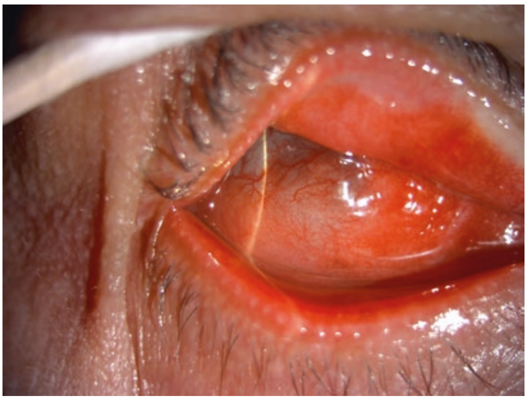

Fig. 9.26 Pseudopterygium covering the cornea, with invisibility of the intraocular tissue in the stable stage (late stage) of chemical burn (Adapted from the photo library of Shandong Eye Hospital, Shandong, China)

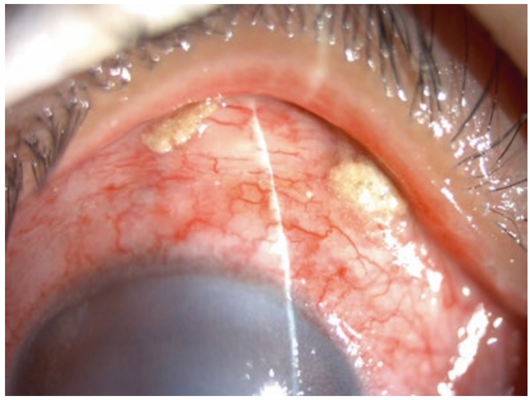

Fig. 9.27 Acute cement burn with solid residues in the superior fornix of the conjunctival sac (Adapted from the photo library of Shandong Eye Hospital, Shandong, China)

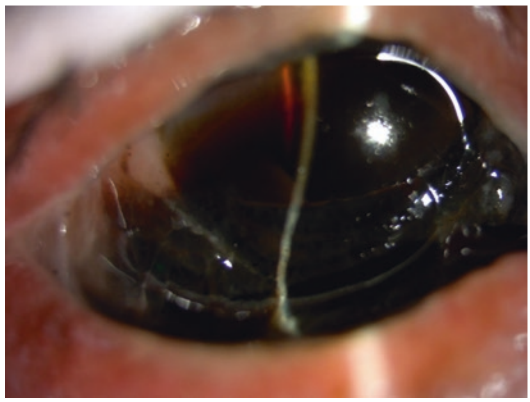

Fig. 9.28 Potassium permanganate powder-induced burn with dark purple staining of the inferior bulbar conjunctiva and cornea and severe conjunctival edema

9.3 First Aid and Treatment of Chemical Injuries

9.3.1 Medical Therapy

9.3.1.1 Emergency Management

- Irrigation of the eye. Eye wash within 3 min after chemical burn is effective for dilution of the harmful chemical substance. Topical anesthesia in the conjunctival sac can be performed first if possible, followed by eyelid opening as much as possible and foreign body removal. Irrigation of the ocular surface for a brief time could only temporarily decrease the pH level. Eye flushing requires at least 30 min for pH neutralization. The use of an eyelid retractor or speculum is helpful during the irrigation. Moreover, a weak acid or alkaline added into the irrigating solution may neutralize the pathogenic chemical substance (Figs. 9.27, 9.28 and 9.29).
- Paracentesis of the anterior chamber. Alkali substance may penetrate the anterior chamber in 3 min but can return to normal within 1–3 h. It is of no clinical significance if the paracentesis is performed after 1 day.
- Bulbar conjunctival incision. A radial incision of the bulbar conjunctiva before irrigation helps to dilute the subconjunctival chemical.
- Use of heparin. Conjunctival vascular embolization and atresia generated by chemical burn

Fig. 9.29 Inferior conjunctival ischemic necrosis observed during amniotic membrane transplantation after irrigation with vitamin C dilute solution

can be treated with heparin for restoring blood circulation. The solution of 1000–2000 units per ml is usually topically administered every 15–30 min for 3–5 days, until the limbal blood vessels become dilated. The presence of bloodlike tears means improvement, and drug withdrawal is not needed.

9.3.1.2 Use of Soft Corneal Contact Lenses

Soft contact lenses stimulate the repair of the ulcer surface and epithelium. However, the oxygen supply to the cornea is reduced, and the chance of infection is increased during lens wear, so the use is not common at present.

9.3.1.3 Corticosteroids

Corticosteroids can not only reduce inflammation and inhibit the proliferation of capillaries but also stimulate collagen activity and increase the dissolution of corneal tissue. Improper use may lead to corneal perforation. It is important to understand the pathological process of alkali burn before choosing medication timing to play the advantages of steroids and reduce the incidence of complications. If there is no obvious corneal ulcer within 1 week after the burn, topical and systemic use of corticosteroids is recommended for reduction of inflammation. After 1 week, topical corticosteroids can be tapered or stopped, with nonsteroidal drugs instead.

9.3.1.4 Collagen Agents

Administration of 0.2% EDTA may play a role in preventing corneal lamellar dissolution.

9.3.1.5 Prevention of Infection

Local and systemic use of antibiotics is recommended.

9.3.2 Surgical Management

9.3.2.1 Amniotic Membrane Transplantation

- Indications: Amniotic membrane transplantation seems to be the most effective approach to chemical burn. Regardless of the severity, when there are corneal limbal ischemia and epithelial abnormality in the acute stage, amniotic membrane transplantation can be performed, the sooner the better [9–11].
- Surgical procedure: Foreign bodies and necrotic tissue of the conjunctival surface and sac are removed, before the necrotic corneal epithelium and stroma are scraped. Glycerin-preserved human amniotic membrane, 2 cm x 3 cm in diameter, is spread on the corneal and conjunctival surface and sutured continuously at 1 mm inside the corneoscleral limbus with a 10–0 nylon suture. The ischemic area in the conjunctiva is also covered with amniotic membrane, which is fixed at 3 mm outside the limbus with interrupted sutures, and then the extra amniotic membrane is cut off. For patients with conjunctival or scleral ischemia, a strabismus hook can be used to massage the ischemic region after the bulbar conjunctiva is cut open for recovery of partial blood vessel occlusion. When there is deep corneal ulceration or perforation, the superficial necrotic tissue is removed, after which a double layer of amniotic membrane is used for repair, and another layer of amniotic membrane is sutured on the surface. For patients with combined symblepharon, separation of the adhesion and fornix reconstruction may be performed simultaneously, with the amniotic membrane fixed to the fornix (Figs. 9.30, 9.31, 9.32, 9.33, 9.34, 9.35, 9.36, 9.37, 9.38, 9.39 and 9.40).

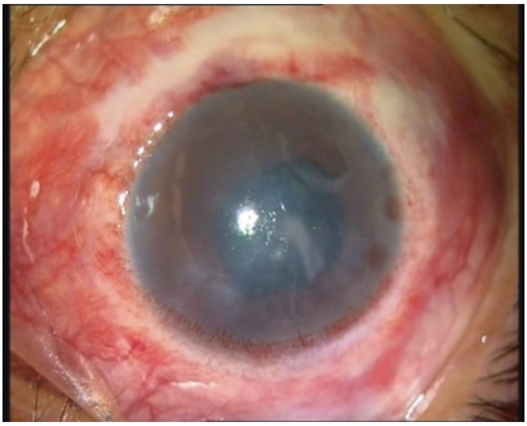

Fig. 9.30 Ischemia of the partial conjunctiva and epithelial erosion, stromal edema, and macular nebulae of the cornea at 10 days after ammonia burn

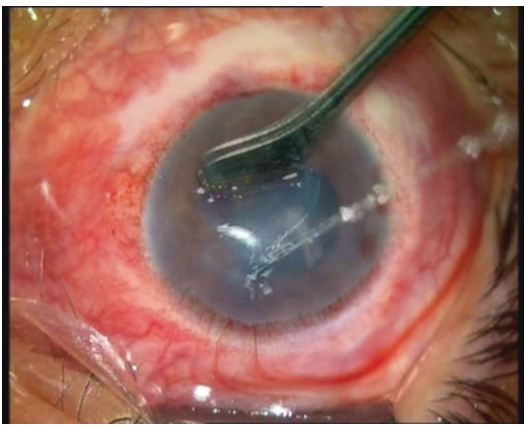

Fig. 9.31 Scraping of the denatured and necrotic corneal epithelial tissue with a blade

Fig. 9.32 Presentation of the basically transparent cornea with localized macular nebulae in the stroma, posterior synechia of the iris, and the out-of-round pupil after epithelial scraping

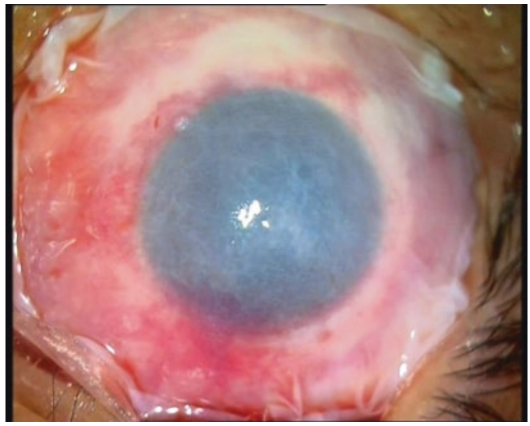

Fig. 9.33 Covering of glycerin-preserved amniotic membrane on the ocular surface with the basement membrane contacting the recipient cornea and conjunctiva

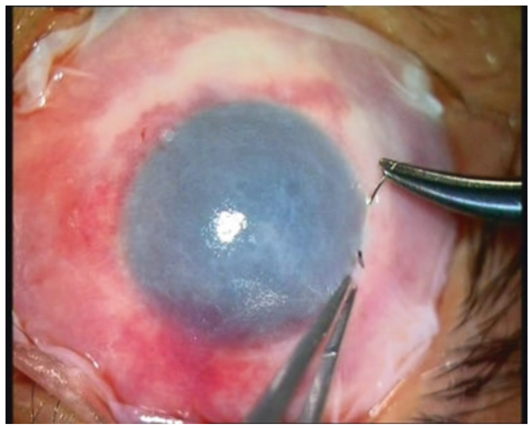

Fig. 9.34 Insert a needle from the 9 o'clock position at the corneal limbus with 1/2 to 2/3 corneal thickness. Note the insertion should be close to the limbal blood vessels but not the clear cornea for prevention of postoperative leukoma

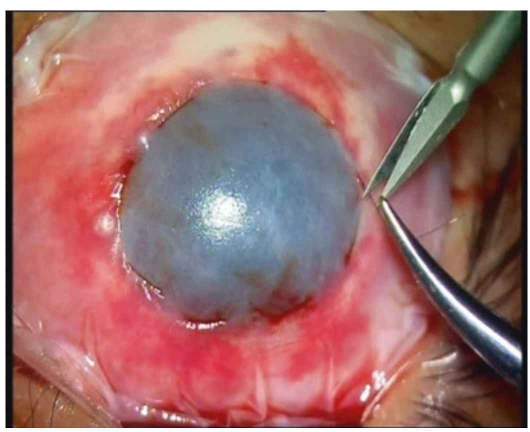

Fig. 9.35 Suture along the corneal limbus with a 10-0 nylon suture and tie a knot before cutting off

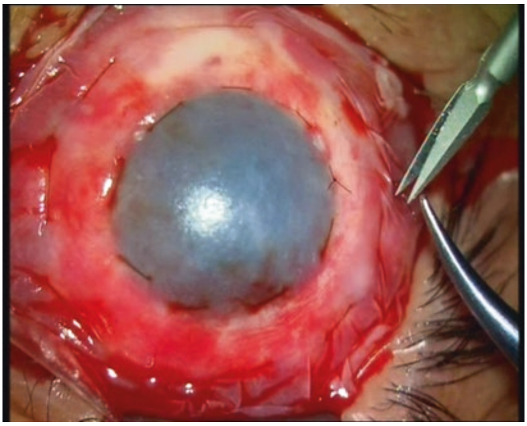

Fig. 9.36 Suture at 5 mm to 8 mm outside the corneal limbus with a 10-0 nylon suture and tie a knot before cutting off

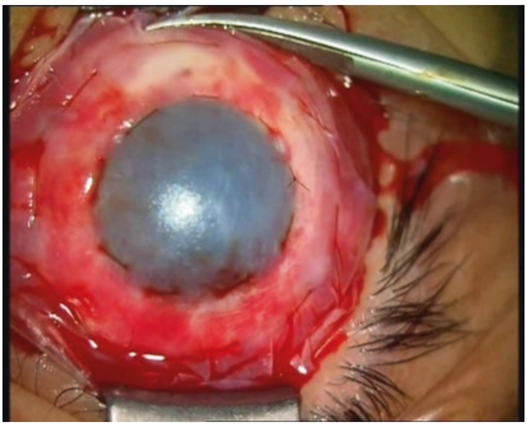

Fig. 9.37 Cut the extra amniotic membrane at 2 mm outside the outer suture with scissors

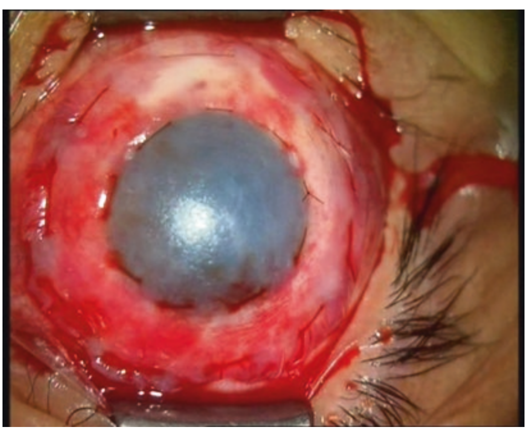

Fig. 9.38 Tight adhesion of amniotic membrane to the ocular surface after double continuous sutures despite hyphema of the tissue below

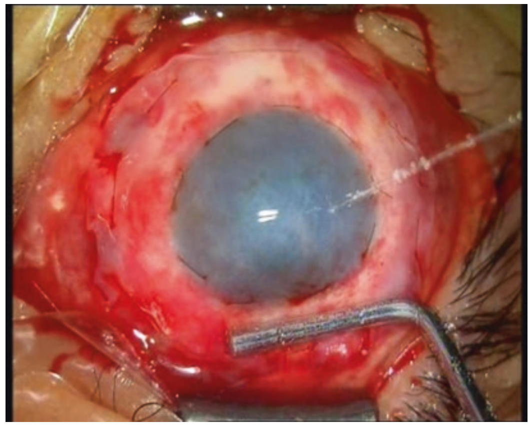

Fig. 9.39 A strabismus hook is gently and radially pushed on the surface, from the center to the periphery, to clear the hyphema under the amniotic membrane after eye rinse with saline solution

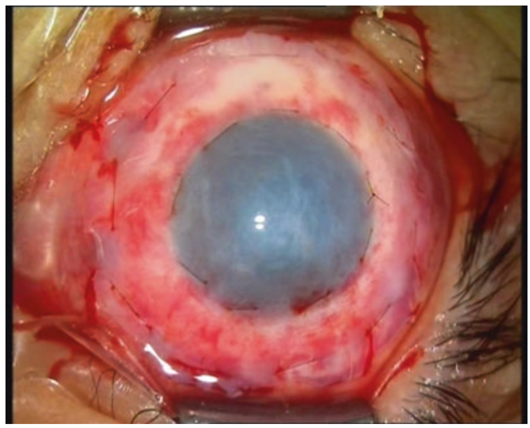

Fig. 9.40 Amniotic membrane attaching to the ocular surface closely after double continuous sutures

- Postoperative treatment: Early after surgery, antibiotic and corticosteroid eye drops are administered, with the dosage and time of steroids adjusted based on the corneal epithelial healing and dissolution, and patients with conjunctival ischemia are also treated with heparin eye drops. The attachment of amniotic membrane needs to be monitored in case of effusion, hyphema, or dissolution of the amniotic membrane. Once the amniotic membrane dissolves, removal of the amniotic membrane should be carried out. If the epithelium does not heal, a second amniotic membrane trans-

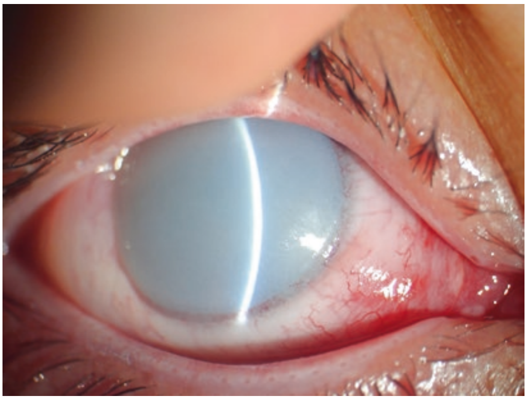

Fig. 9.41 Acute alkali burn of grade IV with extensive ischemia and vascular occlusion of the bulbar conjunctiva, epithelial defects, opacity and edema of the cornea, and invisible intraocular tissue

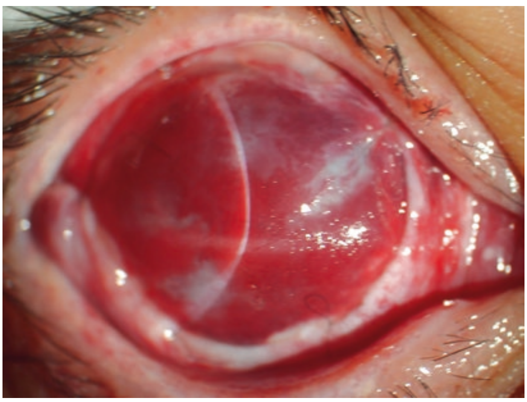

Fig. 9.42 Massage the ischemic region after the bulbar conjunctiva is cut open during amniotic membrane transplantation. Postoperatively, heparin is used to improve the blood circulation, and hyphema occurs under the transplanted membrane

plantation can be performed. For patients developing corneal dissolution, double-layer amniotic membrane transplantation or conjunctival flap covering can be employed, but if the ulcer is deep, or descemetocele and even corneal perforation occur, keratoplasty is required (Figs. 9.41, 9.42, 9.43, 9.44, 9.45, 9.46 and 9.47).

Fig. 9.43 After the discharge of hyphema under the amniotic membrane with a glass rod

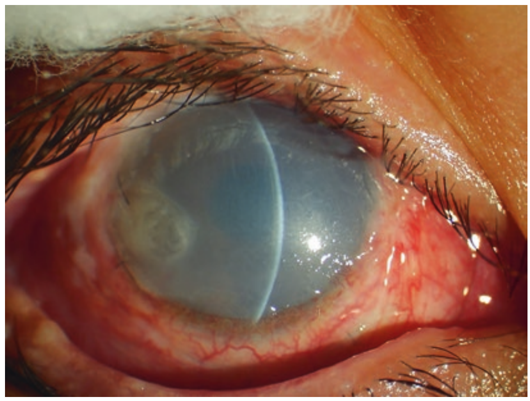

Fig. 9.44 Improved corneal transparency but epithelial non-healing with temporal corneal ulceration and dissolution after the third amniotic membrane transplantation

9.3.3 Autologous or Allogeneic Corneal Limbal Stem Cell Transplantation

- Indications include the ocular burn in the repair stage and corneal limbal stem cell decompensation but transparent stroma.
- Surgical principles: For unilateral injury, transplantation of corneoscleral limbal stem cells from the contralateral healthy eye is performed, while for bilateral injury, allogeneic corneal limbal stem cell transplantation is required.

Fig. 9.45 Corneal ulceration uncontrollable by amniotic membrane transplantation continues to expand and dissolve and fails to be treated by permanent tarsorrhaphy

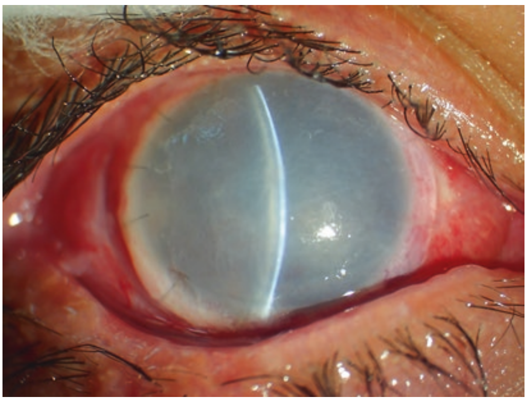

Fig. 9.46 Total lamellar keratoplasty for preservation of the eye globe

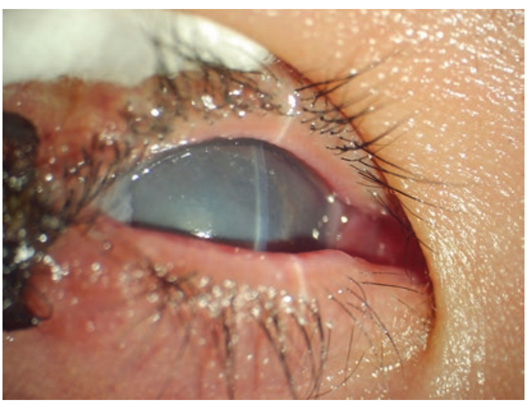

Fig. 9.47 Healing of the corneal epithelium after a second permanent tarsorrhaphy due to slow epithelial recovery

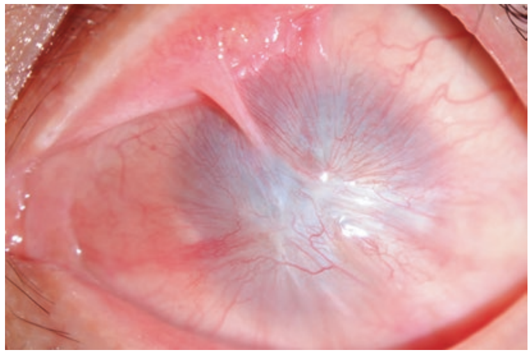

Fig. 9.48 Superior symblepharon, pseudopterygium covering the cornea, and invisible intraocular tissue in the stable stage (late stage) of chemical burn

Autologous limbal stem cell transplantation. Pseudopterygium and new blood vessels are resected, before contralateral corneal limbal stem cells with the conjunctiva are transplanted. The limbal graft obtained from the healthy eye usually should not be more than 1/3 of the corneoscleral limbus.

Ring-shaped corneal limbal stem cell transplantation. When the corneal limbus is completely destroyed, the corneal surface is covered with a large number of new blood vessels, but the corneal stroma is basically normal. In eyes with good transparency, corneal pannus resection is performed, followed by circular bulbar conjunctival incision. A fresh circular corneoscleral rim bearing limbal stem cells is prepared with trephination of the transparent central cornea using a 9 mm trephine. Then an annular graft with 1 mm clear corneal tissue, corneoscleral limbus, and 1 mm scleral tissue is obtained, 50 μm to 80 μm in thickness, and sutured interruptedly to the recipient cornea and sclera. The main postoperative measurement is to prevent immune rejection (Figs. 9.48, 9.49, 9.50, 9.51, 9.52, 9.53 and 9.54).

9.3.4 Lamellar Keratoplasty Combined with Corneal Limbal Stem Cell Transplant

Surgical treatment of the late complications includes corneal limbal stem cell transplantation, global adhesion separation and formation, lamel-

Fig. 9.49 Allogeneic limbal stem cell transplantation is performed when the corneal stroma is found to be clear after dissection of the pseudopterygium

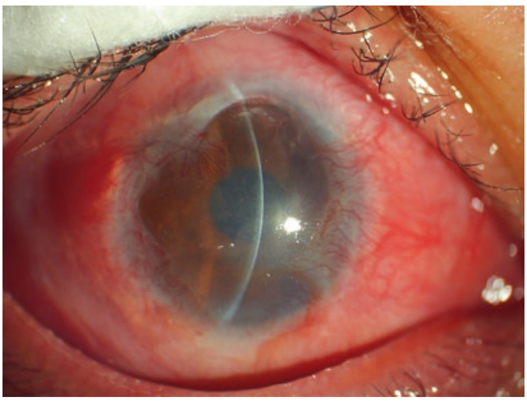

Fig. 9.50 Conjunctival scarring and new blood vessels of the corneal limbus growing into the cornea at half a year after acid burn

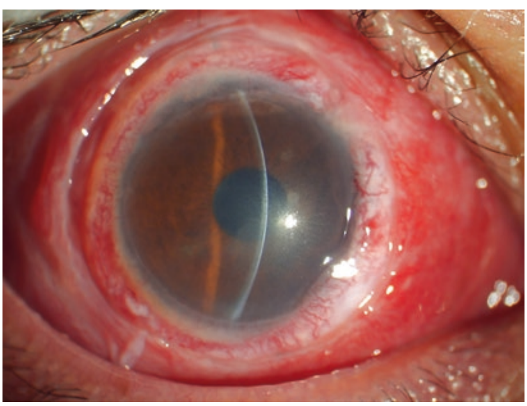

Fig. 9.51 Corneal stromal transparency and epithelial healing after ring-shaped limbal stem cell transplantation

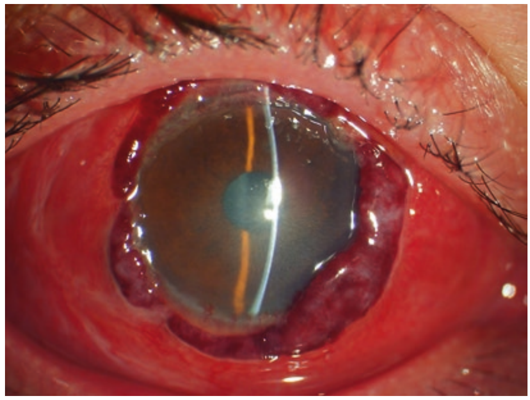

Fig. 9.52 Immune rejection at postoperative 2 months with eye redness as well as dark red congestion and protuberation of the corneoscleral limbus

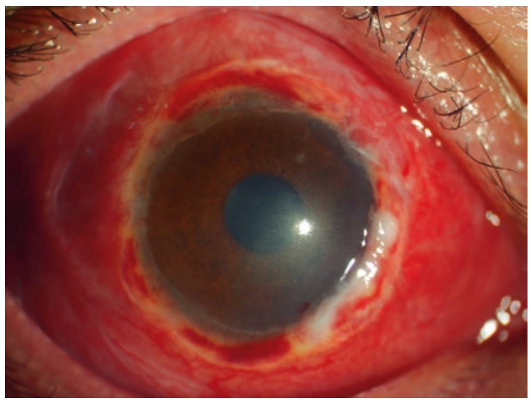

Fig. 9.53 Alleviated corneal limbal congestion after 2 weeks of antirejection treatment

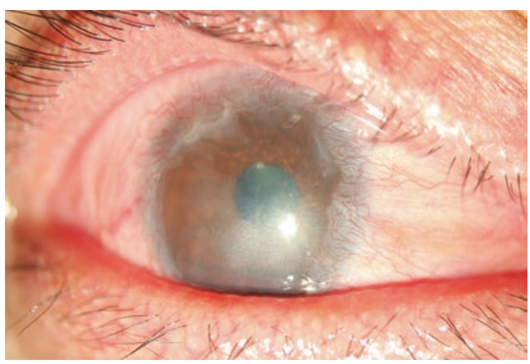

Fig. 9.54 Corneal limbal congestion subsiding and pannus regrowth after 6 months of antirejection treatment

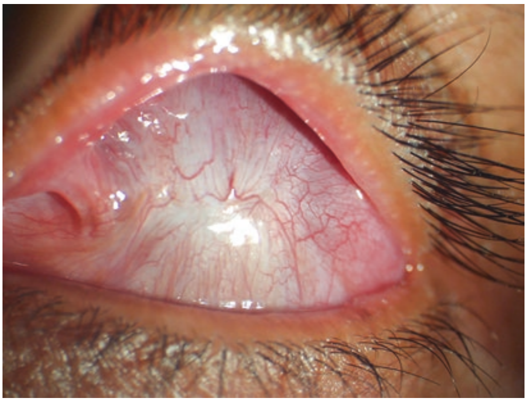

Fig. 9.55 Symblepharon at 6 months after alkali burn

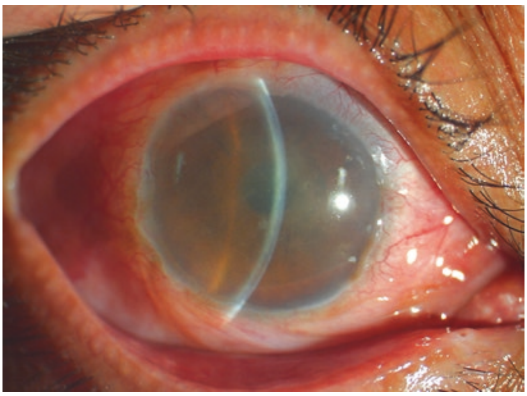

Fig. 9.56 Stable ocular surface at 6 months after total lamellar keratoplasty and reconstruction of the conjunctival sac with autologous conjunctiva and amniotic membrane

lar keratoplasty, penetrating keratoplasty, penetrating keratoplasty combined with stem cell transplantation, and total corneal transplantation with the corneoscleral limbus [12, 13].

- Indications of lamellar keratoplasty include corneal limbal stem cell decompensation with stromal opacity in the repair stage of ocular burns and severe symblepharon (Figs. 9.55 and 9.56) [14–16].
- Surgical principles: The bulbar conjunctiva is incised along the limbus, and the subconjunctival tissue is mildly separated and pushed back around 2 mm. After resection of more than 3/4 thickness of opaque corneal tissue, the intact part of the corneal limbus is remained. Then a total lamellar corneal tissue with limbal girdle of Vogt and intact epithelium, which is preserved in the eye bank for less than 24 h, is transplanted.
- Surgical procedure: First, separation of symblepharon, relief of global bondage, and isolation and preservation of pseudopterygium are performed. Second, partial lamellar keratoplasty with the corneoscleral limbus is employed for patients with adhesion graded III. If the pupil is involved, a mark of corneal trephination can be made across the pupil area and away from the healthy limbus on the other side. Then an adjustable diamond knife is used to cut along the mark through 1/2 to 3/4 thickness of the cornea, before the denatured tissue and new blood vessels are resected layer by layer to achieve a transparent recipient bed. A donor eye globe preserved in the moist chamber for less than 24 h is used to prepare a corneal graft with the corneoscleral limbus. After adequate hemostasis of the recipient bed, the graft is placed and sutured with interrupted 10-0 nylon sutures. Total lamellar keratoplasty is performed for patients with adhesion graded IV. The graft has the whole circular corneoscleral limbal tissue. Third, to reconstruct the conjunctival sac, the separated pseudopterygium is recessed and fixed to the sclera with a 10-0 nylon suture. According to the size of the wound, a conjunctival flap with the corneal limbus (no more than 1/4 of the limbus in the healthy eye) is obtained from the contralateral eye, put on the affected conjunctiva, and sclerally sutured with a 10–0 nylon suture.
- Postoperative treatment: Eye drops of corticosteroids, 1% cyclosporine A or tacrolimus, and artificial tears are administered. Oral steroids are also used. In patients with an allograft larger than 1/2 of the limbus, cyclosporine A capsules are added.
- Postoperative corneal interface fluid, hyphema, or immune rejection can be treated correspondingly. Epithelial defects can be managed by covering the eyes with topical

antibiotic ointment. For refractory non-healing of the epithelium, temporary or permanent tarsorrhaphy is considered.
- Surgical tips: First, pseudopterygium, which can partially replace the bulbar conjunctiva, is used to reconstruct the conjunctival sac in combination with the autologous conjunctiva and transplanted amniotic membrane. Second, autologous limbal stem cells should be retained as long as some function remains. Third, staged surgery is better for large-scale symblepharon. If adhesions are completely separated by one single surgery, usually there is no adequate substitute for wound repair, which inevitably leads to adhesion recurrence. To achieve the expected results, separation of symblepharon can be performed with more than one surgery.

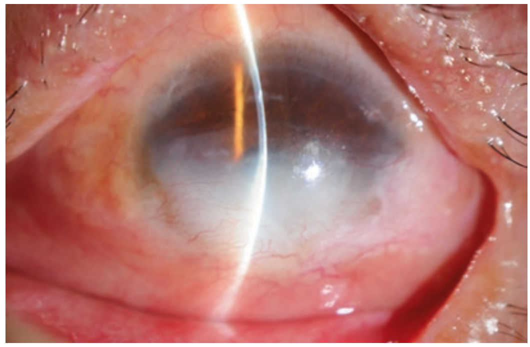

Fig. 9.57 Old alkali burn with inferior corneal opacity and neovascularization

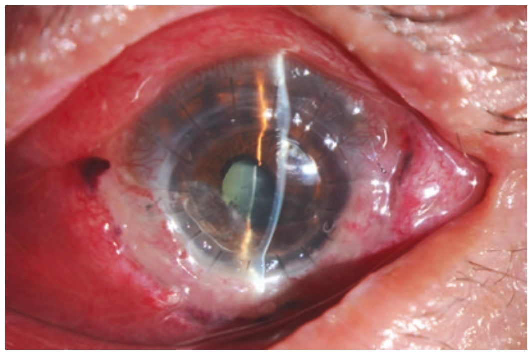

Fig. 9.58 Two weeks after penetrating keratoplasty combined with ring-shaped limbal stem cell transplantation

9.3.5 Penetrating Keratoplasty Combined with Keratolimbal Allograft Transplantation for Severe Burns of the Cornea

- Indications: Patients with severe burns of the cornea in the late stage often suffer full-thickness corneal opacity with neovascularization and even blindness due to devastating damage to the corneal and limbal stem cells. Simple penetrating keratoplasty, lamellar keratoplasty, or keratolimbal allograft transplantation is not able to tackle the problems of both corneal opacity and limbal stem cell decompensation at the same time. Anterior segment reconstruction (total corneal transplantation with the corneal limbus) can be performed, but the disadvantages are high rates of postoperative complications and immune rejection and poor long-term effects. Penetrating keratoplasty combined with keratolimbal allograft transplantation is a promising surgical approach, which can not only treat corneal opacity and limbal stem cell damage but also reduce complications and immune rejection [17, 18].
- Surgical procedure: The transplanted cornea is obtained from young donors within 6 h post mortem and preserved in the intermediate-term corneal storage medium. Pseudopterygium on the corneal surface is resected first, before the conjunctiva is incised along the corneoscleral limbus. Penetrating keratoplasty is performed, with trephination of 7.25 mm or 7.5 mm. The donor cornea is 0.25 mm larger than the recipient bed. Then a ring-shaped keratolimbal allograft, obtained from the same donor, is also transplanted, with an inner diameter of 9 mm and an outer diameter of 15 mm. Approximately 4/5 thickness of the corneoscleral stroma is dissected, and the annular graft is sutured to the recipient limbal area with interrupted 10-0 nylon sutures inside and outside the ring (Figs. 9.57, 9.58 and 9.59).

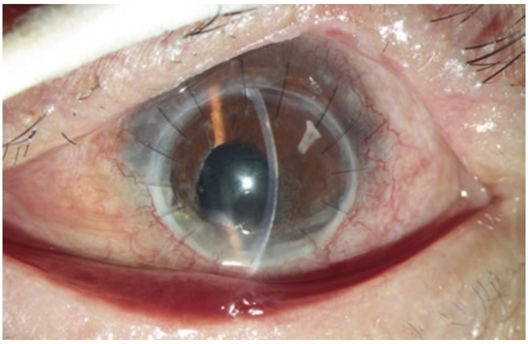

Fig. 9.59 Clear graft and stable ocular surface at 14 months after penetrating keratoplasty combined with keratolimbal allograft transplantation

- Postoperative follow-up and treatment: Systemic corticosteroids and immunosuppressants are used in combination with topical corticosteroid eye drops and cyclosporine or tacrolimus eye drops. The interval of follow-up is 1 month for the first postoperative year and prolonged thereafter. Corneal epithelium and immune rejection are monitored.

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Emergency of Ocular Adnexa

10

Haoyu Chen, Dan Chao, Guihua Xu, Chen Lin, and Zeyi Li

Abstract

Injuries to the ocular adnexal structures also need emergency care. Eyelid lacerations can be partial or full thickness, with or without tissue loss. The wounds should be cleaned, foreign body should be removed, and the lacerations of eyelid should be closed layer by layer. Lacrimal injury can induce dislocation and obstruction of lacrimal passage; therefore, it should be sutured and a supporting tube should be placed. Patients with orbital fracture may present impairment of eye movements and enophthalmos. Surgery is needed to restore the anatomy of orbit. Traumatic optic neuropathy may lead to variable severity of visual acuity loss ranging from normal to no light perception. Although corticosteroid and surgical decompression were reported to treat traumatic optic neuropathy, there is no randomized control trials supporting they can provide additional benefit compared to observation alone.

Keywords

Ocular adnexa injury · Eyelid trauma · Injury of the lacrimal system · Orbital fracture · Traumatic optic neuropathy

10.1 Eyelid Trauma

Eyelids are important structures protecting the eyeballs from mechanical, chemical, and physical injury. Eyelids also maintain the integrity of tear film and help to drain the tears through the lacrimal drainage system. The eyelid structures include the skin, muscles, connective tissue, and mucous membrane. Trauma to the eyelid can cause damage to these structures. Studies have shown that injuries to the eyelids comprise up to 13% of anatomical regions involved [1]. Among all cases of eyelid trauma, the lid margin is affected in 24% and the lacrimal drainage system in 16% of all injuries [2].

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Eyelid trauma can be caused by blunt or penetrating force. Blunt trauma may result from various causes such as traffic accident, assault, play or sports, or a fall, while sharp objects or animal bites can result in laceration or penetrating eyelid trauma.

Eyelid injuries vary in severity and extent and present in a different fashion. Presentations of blunt trauma of the eyelid include skin abrasions/bruises/subcutaneous bleeding/subcutaneous emphysema/hematomas. Eyelid lacerations can be classified into (1) partial thickness and (2) full thickness, which can be further classified (a) with or (b) without tissue loss, and (3) complex injury, which is associated with injuries to other structures, including eye/orbital/facial injuries, facial bone fractures, and canalicular injury.

The ocular examination should be performed meticulously before manipulating the injured eye. Site of injury, tissue loss, infection, and injury to the levator palpebrae aponeurosis should be considered when evaluating the extent of eyelid injury. X-ray and CT scan may be required to exclude open-globe injury, intraocular or intraorbital foreign body, and fracture of the orbit and basal skull.

Uncomplicated eyelid contusions are treated with ice packs to decrease tissue swelling during the first 24–48 h, followed by warm compresses to aid absorption of the hematoma. The patients should be instructed not to blow the nose when there is eyelid emphysema.

Due to the functional and cosmetic importance of the eyelid, repair and reconstruction becomes paramount for eyelid laceration or penetrating injury. However, data show a high association (44%) of eyelid injuries with trauma to the globe [3]. Further damage to the eyeball may occur when repairing eyelids on an open globe. Therefore, repair of the eyeball should take precedence over eyelid laceration repairing.

Eyelid trauma should be addressed within 24 h as primary repair. However, if there are life-threatening systemic injuries, the primary repair can be delayed for 3–5 days. In this case, the wound of the eyelid should be kept clean. Antibiotics should be prescribed to prevent secondary infection. In case of animal bites, antibiotic cover and meticulous cleaning are needed, and proper immunization should be given if required. Give tetanus immunization if needed.

Most eyelid injuries can be repaired under local anesthesia. General anesthesia is only required in uncooperative patients or children. Intraoperatively, the wounds should be cleaned and foreign body should be removed from the wound. Eyelid lacerations should be closed layer by layer. Minor lid lacerations not involving the lid margin or tarsal plate may be repaired with 6-0 or 7-0 nylon sutures. Eyelid lacerations involving the lid margin need careful repair. Imperfect suturing will result in notching and ocular surface problems postoperatively. Complicated lid lacerations with tissue loss may need a reconstructive procedure. The amount of tissue loss determines the surgical outcome. As a general rule, intubation of the canaliculus should be performed before the repairing of laminal canthus [4]. Lacerations which involve the levator palpebrae aponeurosis can cause ptosis and might require specific surgery at a later date.

10.1.1 Case Presentation

A 22-year-old male was injured in a traffic accident. Both upper and lower eyelids were severely lacerated (Fig. 10.1a). Primary repair was performed (Fig. 10.1b). Three months postoperatively, ptosis was notable (Fig. 10.1c).

Fig. 10.1 A case with eyelid laceration. (**a**) Before operation; (**b**) Three days after operation; (**c**) Three months after operation

10.2 Injury of Lacrimal System

Lacrimal injury is mostly caused by impact and sharp injuries (e.g., animal bites). Lacrimal injury includes membranous lacrimal injury and bony lacrimal injury. Membranous lacrimal injury can occur in the lacrimal duct and lacrimal sac; bony lacrimal injury can occur around the lacrimal sac and nasolacrimal duct. Bone displacement and fragments can induce tear or rupture of the mucosa of the lacrimal sac and nasolacrimal duct, as well as fracture of the nasal and nasal orbital sieve.

Inappropriate repair of lacrimal injury can induce dislocation and obstruction of lacrimal passage. The obstruction of the lacrimal duct and lacrimal canaliculi will result in epiphora, whereas obstruction of the lower lacrimal sac or nasolacrimal duct will frequently result in chronic dacryocystitis and cause epiphora and pyorrhea.

Diagnosis of lacrimal injury includes the following steps:

- Lacrimal canalicular rupture. This is located near the inner canthus. Lacrimal flush needle or probe can be used to locate the broken end.
- Dacryocyst injury. This involves severe rupture at the inner canthus. Lacrimal flush needle or probe can reach the bone wall. The rinse solu-

tion will overflow from the lacrimal sac area or into the subcutaneous tissue. Intraoperative exploration can find the ruptured lacrimal sac.

- Fracture of lacrimal fossa or nasolacrimal duct area. This occurs due to heavy impact at the nasal or inferior orbital area. Local deformity can be observed. CT scan will show the local fracture of the lacrimal sac or nasolacrimal duct area. Lacrimal passage irrigation or probing will show the obstruction of inferior lacrimal passage.

Management of lacrimal system injury:

- Lacrimal punctum laceration. It should be sutured and a supporting tube should be placed for at least 1 month to avoid occlusion of puncta.
- Lacrimal canalicular rupture. Fresh rupture of the superior lacrimal canaliculus should be repaired if it is possible whereas the inferior lacrimal canaliculus rupture must be repaired. Three-pin suture anastomosis of the lacrimal canaliculus is commonly used. Supporting tube must be placed after the anastomosis for at least 3 months to avoid obstruction of lacrimal canaliculus. The inner canthus and eyelid should reach anatomical reduction to avoid eversion of the eyelid and punctum. For old rupture or obstruction of the lacrimal canaliculus, the obstruction tissue should be cut open to expose the inside end of the lacrimal canaliculus followed by anastomosis of the canaliculus. Various techniques can be used for retrograde detection of the lacrimal canaliculus [5, 6]. Supporting tube must be placed for at least 3 months.
- Dacryocyst injury. Fresh injury (within 3 days) should be sutured properly. In order to avoid adhesions or collapse of dacryocyst, appropriate amount of viscoelastic material can be injected from the lacrimal punctum into the dacryocyst after suturing. The supporting tube can be inserted for 2 weeks to help tear drainage. For old dacryocyst injury, chronic dacryocystitis, or lacrimal sac cyst, as well as bony abnormalities in the lacrimal fossa, dacryocystorhinostomy or dacryocystoplasty should be performed.
- Nasolacrimal duct injury. For fresh injury, fracture reduction can be attempted. If the lacrimal duct can be probed, the supporting tube should be placed for 3 months. For old injury, dacryocystorhinostomy should be performed. Laser lacryocystoplasty is not suggested for this kind of injury.
- Compound injury. For severe compound injury, autologous blood vessels or other artificial material can be used to reconstruct membranous lacrimal passage.

10.2.1 Case Presentation

A 59-year-old male's left eye was injured by an iron hook during work. Physical examination shows laceration of the lower eyelid and lacrimal canaliculus (Fig. 10.2a). The laceration was carefully repaired. Three months after the operation, the lacrimal canaliculus was open after removal of the supporting tube (Fig. 10.2b).

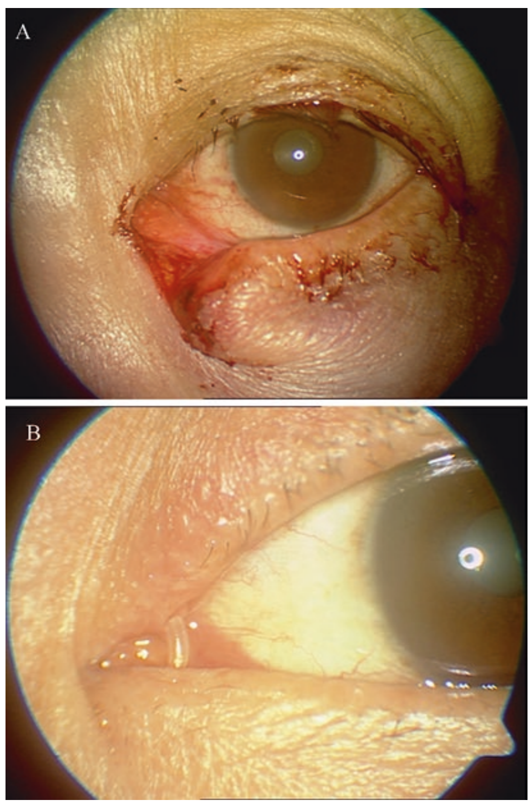

Fig. 10.2 A case with lacrimal canaliculus. (**a**) Before operation; (**b**) Three months after operation

10.3 Orbital Fracture

There are two common types of orbital fractures, trapdoor-type fracture and open-type fracture. The trapdoor-type fracture is seen in young patients with soft bones. It is more likely to restore to its original position. This would result in entrapment of extraocular muscle and orbital fat at the site of fracture, while open-type fracture is commonly seen in adults. The bone is more likely to break completely and dislocate into the sinus around the orbit.

Orbital trauma results from blunt or penetrating trauma. The direct insult and/or indirect pressure transmitted to the orbital bone results in fracture. The medial wall and the orbital floor are the most common sites of fracture, while the orbital roof and the lateral wall are less common because they are thicker and require more force [7]. The medial wall of the orbit is the thinnest wall and consists of the orbital plate of the ethmoid, frontal process of the maxilla, body of the sphenoid, and the lacrimal bone. It is adjacent to the ethmoid sinus. The inferior wall (orbital floor) is formed by the maxilla, the zygomatic bone, and the minute orbital process of the palatine bone. It is located adjacent to the maxillary sinuses. The lateral wall consists of the zygomatic, and it is the hardest and thickest wall and is more resistant to mechanical trauma. The superior wall (orbital roof) consists of the frontal bone and is close to the brain. Therefore, patients with fracture of the orbital roof should consult with a neurosurgeon for potential intracranial injury.

There are many different types of tissue in the orbit, including extraocular muscles, cranial nerves, arteries, veins, and fat tissue. Orbital fat provides support to other tissues within the orbit. In blowout fracture of the orbital wall, the extraocular muscle and orbital fat would dislocate and fix at the site of fracture. This would limit the movement of the eyeball. Injury of cranial nerves and blood vessels would result in specific symptoms according to the injury site.

10.3.1 Clinical Manifestations

The patients with orbital injury may suffer from diplopia. The symptom disappears if one eye is covered. Occasionally, some patients may develop nausea and vomiting due to oculocardiac reflex by stimulation of the orbital branch of the vagus nerve.

During physical examination, impairment of eye movements and enophthalmos are the two most common findings. Impairment of eye movement is caused by dislocation of the extraocular muscle and orbital fat at the site of fracture and, in some rare cases, secondary to damage to the nerve and blood supply. Comprehensive examination of severity of eye movement impairment will help to decide whether and when to perform a surgical intervention. Enophthalmos is due to the dislocation of intraorbital tissues, including orbital fat and extraocular muscles into the sinus, or enlargement of orbital volume in cases of lateral wall fracture. Enophthalmos is an indication of surgery if it is severe and affects the appearance of the patients.

CT scan is useful for investigation and diagnosis of orbital factures. Although transverse plane is the most commonly used view, it provides less useful information for the superior and inferior walls of the orbit. The coronal plane can demonstrate all the four orbital walls in a single image. It also shows the two eyes in the same image for comparison. There are two kinds of images, bone image and soft tissue image. It is recommended that the physician should read the soft tissue images because it can also demonstrate the relationship between the orbital fat, the extraocular muscles, and the orbital walls. Dislocation of bones can be observed on bone images.

10.3.2 Treatment

The timing of surgical intervention depends on the types of fractures and the severity of the symptoms. For trapdoor fractures, emergent sur-

gery should be performed because the incarceration of the extraocular muscle may lead to disruption of blood supply and irreversible damage to the extraocular muscles. For open-type fractures, surgical intervention is recommended 1–2 weeks after the fracture.

The goal of the surgery is to restore the anatomy of the orbit. The herniated extraocular muscle and orbital fat should be released and restored. The fractured bone can be restored in a trapdoor fracture if there is no fragment and the original bone can cover the break completely. Otherwise, if there are orbital bones fragmented by trauma, artificial materials should be used to repair the break in the orbital bone and prevent recurrence of herniation.

10.3.3 Case Presentation

A 23-year-old female was injured in a traffic accident. CT scan demonstrated fracture of lateral and inferior walls of the orbit (Fig. 10.3a–c). The patient received titanium plate implant for orbital fracture reconstruction (Fig. 10.3d, e)

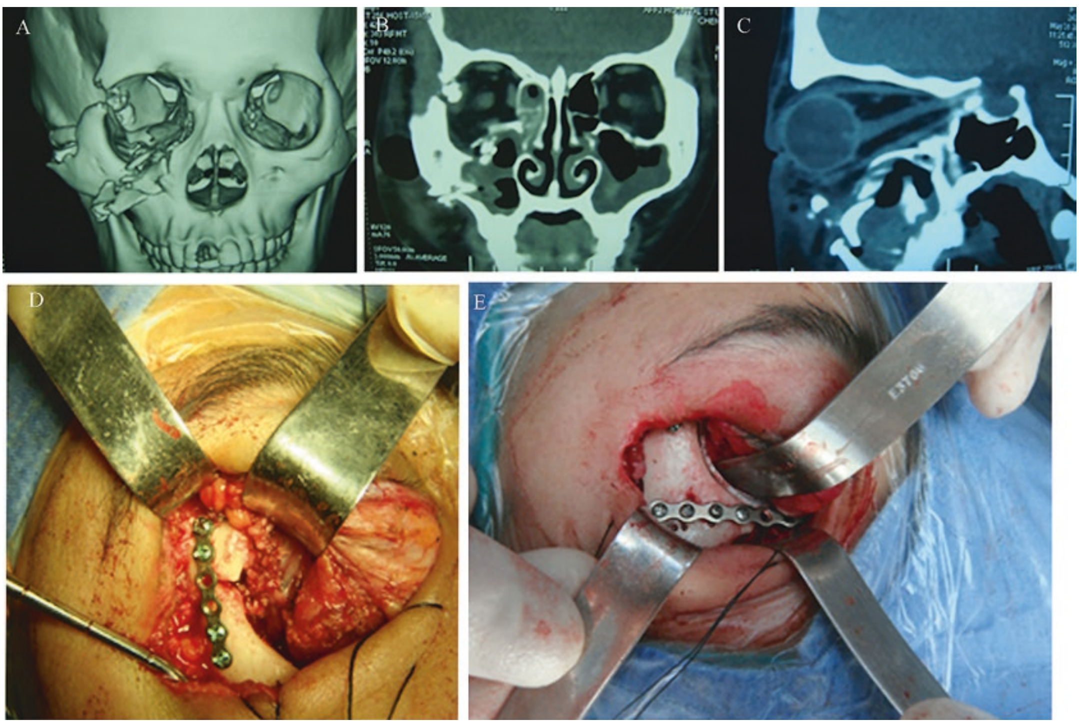

Fig. 10.3 A case with orbital wall fracture. (**a**–**c**) CT scan images; (**d**, **e**) Titanium plate implantation

10.4 Traumatic Optic Neuropathy

Direct or indirect injury to the optic canal can result in optic canal fracture and intracanalicular traumatic optic neuropathy (TON) consequentially. Young male patients in their early thirties are the most commonly affected. The most common causes of traumatic optic neuropathy in adults include traffic accidents, falls, and assaults [8, 9]. In children, fall and road traffic accidents are the leading causes for TON [10].

Optic canal is a bone-base canal, with the dura mater surrounding the optic nerve adherent tightly to the periosteum of the canal, especially at the superior part. Consequently, in patients with direct or indirect blunt trauma, canalicular portion of the optic nerve is the most common site of damage. On one side, the concussive force associated with fractures of the optic canal may be associated with crushing or laceration of the optic nerve; on the other side, any rotational or translational forces of the brain during head and/or facial blunt trauma may play an important role in optic nerve injury portion that crosses underneath the falciform fold. The vulnerability of the canalicular portion of the optic nerve should be taken into account because of its special anatomy. Any edema and hemorrhage may result in a compartment syndrome and cause further ischemia and secondary damage to the optic nerve.

Patients usually have associated damage to the head or face with variable levels of impaired consciousness. Unilateral or bilateral optic nerve involvement may be observed with variable severity of visual acuity loss ranging from mild scotoma to no light perception depending on the severity of optic canal injury. Patients may have color vision impairment, visual field defect, and positive relative afferent papillary defect (RAPD). The appearance of optic nerve head is usually normal at an early stage after the injury but will demonstrate pallor after about 6 weeks following the injury [11–13].

Computed tomography is a useful imaging technique for delineating optic canal fractures. It can clearly show whether there is canalicular fracture or if there is a bony fragment impinging on the optic nerve. If a bone fragment is found impinging on the optic nerve, prompt surgical intervention would be recommended [14]. However, there is no consistent correlation between the presence of optic nerve canal fracture, severity of visual impairment, and visual outcome, with or without surgical intervention. Electrophysiological examination by flash-evoked visual potentials (VEP) and electroretinogram (ERG) is a reliable objective method to investigate the severity of visual pathway function impairment in traumatic optic neuropathy [15, 16].

Due to other life-threatening injuries, an unavoidable delay in ophthalmological assessment is common in the clinic. The main treatment options in optic canal fracture include:

- Intravenous or oral administration of corticosteroids in high doses depending on the severity. The side effects of systemic steroids should be taken into consideration.
- Surgical decompression of optic canal. It depends on the availability of expertise and the surgeon's preference. Postoperative complications such as leakage of cerebrospinal fluid and meningitis must be taken into consideration.
- Combined treatment with steroids and surgery.
- Observation and follow-up.

There is no convincing evidence showing an additional visual benefit of steroids compared to observation alone. Based on a randomized control trial, the visual acuity was not statistically significant after 3 months of follow-up with either choice. For patients with optic canal fracture with bone fragment impingement into the optic nerve, there is no evidence to support the opinion that surgery would benefit these cases. It was reported that the presence of an optic canal fracture is a factor predicting poor visual outcome even when steroids or surgery was used [17–19].

10.4.1 Case Presentation

A 35-year-old male complained of visual impairment after injury in a traffic accident. The best-corrected visual acuity was 20/40. Orbital CT scan revealed lateral wall fracture of the left orbit with an intact optic canal (Fig. 10.4a, b). Visual evoked potential test found reduced response in the left eye (Fig. 10.4c). Visual field test found contraction in the left eye (Fig. 10.4d, e).

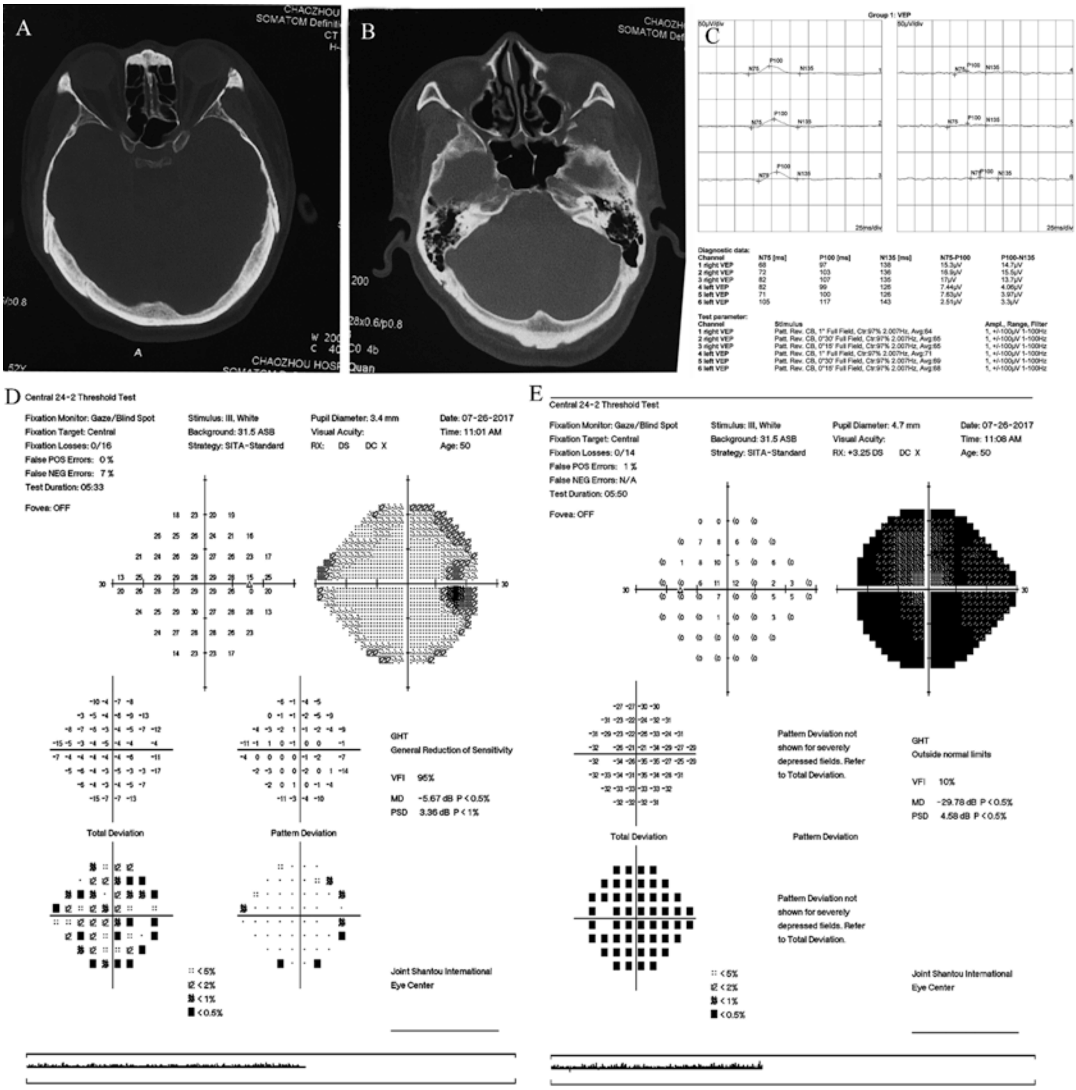

Fig. 10.4 A case with traumatic optic neuropathy. (**a**, **b**) CT scan; (**c**) Visual evoked potential test showed reduced response in the left eye. (**d**, **e**) Visual field test showed contraction in the left eye

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Erratum to: Emergency of Ocular Adnexa

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